Archives of Dermatology and Syphilology

VOLUME 27 FEBRUARY, 1933 NUMBER 2

COMPARISON OF NEOARSPHENAMINE AND ARSPHENAMINE

RESULTS AND REACTIONS IN NINE HUNDRED AND NINETY-NINE PATIENTS UNDER TREATMENT OR OBSERVATION NOT LESS THAN SIX MONTHS

J. P. THORNLEY, M.D.

Attending Specialist in Dermatology and Syphilis, United States Public Health Service; Dermatologist and Syphilographer, Gouverneur Hospital

NEW YORK

There are few diseases in which early and persistent treatment is as uniformly followed by good results as is the treatment of syphilis by the arsenicals.

The fascinating spectacle of lesions, especially those of the skin, which formerly lasted weeks and months, disappearing in a few days like snow before the sun is a source of continuing satisfaction to the syphilographer and probably accounts for the devotion of many to this field of medical endeavor.

This interest and devotion having once been acquired, the fact that the disease is slow, insidious, treacherous and prone to relapse only stimulates one's efforts still further to conquer and control it.

Owing to the well known tendency of syphilis to become latent and then relapse after a long period of time, one must be exceedingly careful in evaluating as a permanent "cure" any form of treatment, the effect of which has not been observed over a long enough period of years and in a large enough number of patients to make average results of real value.

As this is a study of a total number of 5,245 cases, extending over a period of ten years, it is hoped that it will throw some light on the ultimate value of the arsenicals in general and the comparative virtues and short-comings of neoarsphenamine and arsphenamine in the treatment of syphilis.

From the United States Marine Hospital.

Read and published by permission of the Surgeon General, United States Public Health Service.

Read before the Section on Dermatology and Syphilology at the Eighty-Third Annual Session of the American Medical Association, New Orleans, May 12, 1932.

The officers and employees of the United States Public Health Service have given freely of their time and effort in this study.

Owing to the minimum period for observation established, of a total of 5,245 patients with all stages of syphilis treated or observed in this clinic, there are 999 who have been under observation or treatment for a period of six months or longer. This study is an analysis of the reactions to treatment and results in this group.

In estimating the value of any treatment for any disease, the question of ultimate cure is of paramount importance to the individual sufferer. There is an added factor, however, when the disease is contagious. To prevent and minimize the spread of the contagion is of much greater importance to the public at large than is a permanent cure in any individual case.

Thanks to the early disappearance of contagious lesions under treatment, one can say with reasonable assurance that the spread of syphilis has been sensibly retarded. Were this not so, statistics would show an appalling increase instead of an apparent standstill or even a slight decrease.

Unfortunately there are no positive criteria for determining a complete cure. I do not wish to be understood as believing syphilis incurable, or as depreciating the value of the Wassermann test as a diagnostic procedure—far from it. I am of the opinion that not only is syphilis curable, but when there is an attenuated organism and when the patient's resistance is strong, it may be even self-curable. On the other hand, with a virulant infecting agent and weak resistance, a case may well be incurable from the start, and alleviated only by the best of treatment. Between these two extremes all degrees of severity can be and are encountered.

While much attention has been directed to the obstinate, so-called arsenic-fast cases, little attention has been focused on those undoubted cases of syphilis in which little or no treatment is given, yet which seemed to be "cured," even after long observation.

What other explanation is tenable except that the patients manufacture their own curative substance, the very same substance that in severer cases is stimulated to activity by the arsenicals circulated in the blood? It is well known that any safe dose of the arsenicals, when diluted to the extent it must be when circulating in the blood, is not spirocheticidal at all, and that the blood thus treated becomes so only after it has passed through the liver.

The 4 plus Wassermann test is almost 100 per cent perfect in the diagnosis of syphilis, but every one knows that a single negative Wassermann test is no evidence of a "cure," and that a series of negative Wassermann tests is only presumptive evidence of such a result. On the other hand, if the Wassermann test is an evidence of tissue reaction alone, it is not likely that it becomes negative the instant the last spirochete dies. How long this persistence may last is problematic, but

if this idea of the test is true, a patient may well continue to have a positive Wassermann reaction without a single living spirochete in his body.

There is nothing new about the theory just stated; it is simply brought forward to explain why no permanent "cures" are claimed in the tables. There probably were plenty of them, but a clinic devoted to the treatment of sailors is in no position to carry out the modern tests for a "cure" in any satisfactory number of cases.

Even clinics that are able to benefit from perfected follow-up systems can claim only about 12 per cent cures by such standards. This, I think, is misleading. Eighty-eight per cent of failures to cure would be a very poor showing, and I hope and firmly believe that the actual cures are far above 12 per cent. Such an estimate of the percentage of cures by modern standards simply shows that a given clinic can follow up a certain proportion of its cases, and in my opinion, bears no constant relation to the cures actually effected. Therefore, in making up the tables, we have classified our results according to the following definitions, based on serologic and clinical manifestations.

RESULTS

"Cured with negative cerebrospinal fluid" indicates that the patient has been followed for at least one year after the completion of treatment and during this period has had no symptoms of syphilis, no positive Wassermann reactions, a series of negative Wassermann reactions and a negative test of the spinal fluid.

"Cured without negative cerebrospinal fluid" follows the definition already given with the exception that no examination of the cerebrospinal fluid was made on the termination of treatment.

"Probation" follows the definition of "cured without negative cerebrospinal fluid" with the exception that the patient has been followed for *less* than a year after the completion of treatment.

"Relapse and serologic resistance" is a term used to indicate patients experiencing relapses and concerning whom this is the last information available. They have been grouped together, so that a patient having both a clinical and serologic relapse will be shown only once. There are included also in this group those patients whose serology, of either the cerebrospinal fluid or the blood, is resistant to treatment throughout.

"Improved" indicates patients who on their last appearance at the clinic gave negative results in serologic tests, had not experienced a recent serologic or clinical relapse and were still receiving treatment when last seen.

"Unimproved" indicates patients in whom the manifestations of syphilis failed to respond to treatment, as for example, those with tabes dorsalis.

In the accompanying tables satisfactory results include the two classes of so-called cured patients and those on probation and improved. These two last-mentioned results are, of course, satisfactory as far as we know anything about them, but we do not know enough to class the patients as cured. Some will probably be cured and some will not be. But certainly up to the time of the last observation, their condition was satisfactory. Relapses and no improvement constitute the unsatisfactory results.

As we are attempting to establish some sort of comparison in the results of the two drugs under consideration, it will be well to state here that we give a heavy metal, namely, mercury salicylate, in the dose of 1 grain once a week intramuscularly with both neoarsphenamine and arsphenamine, so that whatever changes or differences there may be in the effects of the two drugs must be due to the arsenical and not the mercury.

TABLE 1.—*Comparative Results of Treatment with Arsphenamine and Neoarsphenamine, Used Either Predominantly or Exclusively as the Arsenical*

Results	Patients Treated with Arsphenamine		Patients Treated with Neoarsphenamine	
	Number	Per Cent	Number	Per Cent
Satisfactory	559	68.4	135	77.6
Unsatisfactory	257	31.5	39	22.4
Reinfection	1	0.1	...	....
Total	817*	100.0	174†	100.0

* There are two cases omitted in which the unsatisfactory results occurred at the time neoarsphenamine was being given, although the patient received predominantly arsphenamine.

† There are six cases omitted in which unsatisfactory results occurred during the time arsphenamine was given, although the patient received predominantly neoarsphenamine.

This table reveals that from a serologic standpoint, the results of neoarsphenamine and arsphenamine, as the predominating arsenical, are so close that there is little choice between them.

A word of explanation regarding the small number of patients given neoarsphenamine seems desirable at this point. Neither group of cases has been subjected to any other selection than on the basis of the duration of observation. Neoarsphenamine is given in the morning clinic and arsphenamine in the evening clinic, thus making it practically impossible to make any mistake in the preparation of the two drugs or accidentally to substitute one tube for the other.

The patients themselves are permitted to choose between the night and morning clinics, and are of course influenced by economic pressure. Those who can afford to go without work for six weeks attend the morning clinic, and those who have to work select the night clinic. Naturally the morning attendance is the smaller.

In a still further analysis of the comparative values of neoarsphenamine and arsphenamine as the predominating arsenical, table 2 is given. In it we have shown the results of treatment separately and the number of doses of each kind of arsphenamine with which this result was attained.

COMMENT ON TABLE 2

The comment on table 1 has already indicated the small percentage of patients in whom we were able to make a test of the cerebrospinal fluid after completion of treatment (1.6 per cent of those given arsphenamine and 1.7 of those given neoarsphenamine), because our patients, who are sailors, do not come for a spinal puncture: first, because they do not want to take the trouble, and second, because of the fact that in lodging houses, sailors' club rooms and on board ship they compare notes and are fully conversant with the possibilities of a headache following a spinal puncture.

With this sort of prejudice to deal with, a systematic effort to obtain Wassermann reactions of the cerebrospinal fluid would be almost impossible, certainly in numbers satisfactory enough to be of any service.

Table 2 shows that the proportion of patients receiving varying numbers of injections is quite similar for both arsphenamine and neoarsphenamine. It has already been shown that the satisfactory results with the two drugs when the heavy metals are used concurrently are practically equivalent, the percentage of patients reported as "cured" or "probated" being quite similar for the two groups. However, the number of cases of relapse or serologic resistance is slightly higher among those treated exclusively or predominantly with arsphenamine. Perhaps I should caution the reader against placing too much faith in slight differences in these percentages, since the number of patients treated with neoarsphenamine is comparatively small.

The satisfactory results cannot be attributed wholly to the amount of treatment administered. As a matter of fact, in previous studies it has been found that the continuity of treatment has a great deal more to do with the ultimate effectiveness of treatment than the total number of injections of arsphenamine administered.

A comparative study of the two drugs with respect to the rapidity with which the Wassermann tests were changed from positive to negative shows that with both arsphenamine and neoarsphenamine a permanent reversal to a negative reaction was obtained in three months in 14 and 13 per cent respectively. In approximately 70 per cent of the patients treated with either of these drugs a permanent reversal of the Wassermann reaction of the blood was experienced within a year after the beginning of treatment.

TABLE 2.—*Correlation of Results of Treatment with the Predominating Arsenical Used and the Number of Doses Administered*

Results	1-6 Doses		7-12 Doses		13-18 Doses		19-24 Doses		25-30 Doses		Over 30 Doses		Total		Total	
	No. Cases	Per Cent	No. Cases	Per Cent	No. Cases	Per Cent	No. Cases	Per Cent	No. Cases	Per Cent	No. Cases	Per Cent	No. Cases	Per Cent	No. Cases	Per Cent
Arsphenamine																
Cured with negative cerebrospinal fluid	..	....	4	30.7	..	....	5	38.5	2	15.4	2	15.4	13	100.0	13	1.6
Cured without negative cerebrospinal fluid	20	10.6	85	45.0	18	9.5	27	14.3	11	5.8	28	14.8	189	100.0	189	23.2
Probation	11	6.2	61	34.5	23	13.0	39	22.0	11	6.2	32	18.1	177	100.0	177	21.7
Relapse and serologic resistance	26	10.2	106	41.6	23	9.0	50	19.6	19	7.4	31	12.2	255	100.0	255	31.2
Improved	11	6.1	38	21.1	12	6.7	65	36.1	11	6.1	43	23.9	180	100.0	180	22.0
Reinfection	..	....	..	....	1	100.0	..	....	..	....	..	....	1	100.0	1	0.1
Unimproved	..	....	..	....	..	....	..	....	1	50.0	1	50.0	2	100.0	2	0.2
Total	68	8.3	294	36.0	77	9.4	186	22.8	55	6.7	137	16.8	817*	100.0	817*	100.0
Neoarsphenamine																
Cured with negative cerebrospinal fluid	..	....	1	33.3	1	33.3	..	....	..	....	1	33.3	3	100.0	3	1.7
Cured without negative cerebrospinal fluid	5	11.6	16	37.2	3	7.0	12	27.9	..	....	7	16.3	43	100.0	43	24.7
Probation	1	2.0	19	38.8	3	6.1	11	22.5	2	4.1	13	26.5	49	100.0	49	28.2
Relapse and serologic resistance	3	7.9	20	52.7	1	2.6	7	18.4	3	7.9	4	10.5	38	100.0	38	21.8
Improved	..	....	8	20.0	3	7.5	12	30.0	4	10.0	13	32.5	40	100.0	40	23.0
Unimproved	..	....	..	....	..	....	..	....	1	100.0	..	....	1	100.0	1	0.6
Total	9	5.2	64	36.8	11	6.3	42	24.1	10	5.8	38	21.8	174†	100.0	174†	100.0

* Two cases in which the relapse or serologic resistance occurred during the use of neoarsphenamine are omitted.

† Six cases in which the relapse or serologic resistance occurred during the use of arsphenamine are omitted.

At the Hudson Street Hospital clinic, patients are treated by the continuous method whenever we can induce them to come for it; and I attribute whatever satisfactory results we have obtained in the administration of these two drugs to the intensive education of the patient from the very beginning of the clinic. We leave no stone unturned to make the patients understand the importance of persistent and continuous treatment.

If we divide the total number of arsenical injections which we have given in the past ten years by the total number of patients, we find that we have had an average of twelve injections of arsphenamine per patient. The public health import of this fact has been very strongly brought out in a recent paper on mucocutaneous relapse, which revealed that, with nine or more injections of arsphenamine, the patients with early syphilis were only one-fifth as apt to have a clinical relapse as they would be if they received five injections or less.

REACTIONS

The study of reactions is almost as important as is the study of the beneficial results of treatment.

They frequently seriously interfere with an orderly routine and often force one to use less efficient drugs. Therefore their avoidance is of the utmost importance.

While this article is a study of cases that have been under observation for six months or longer, we must not lose sight of the fact that a large proportion of reactions occur early, and that patients who have reactions early are liable to abandon treatment or be put on less effective medication, long before six months have elapsed. Therefore the figures and conclusions here set forth may have to be materially altered after we have studied all of the reactions and all the complications occurring in all our cases during the past ten years.

Of the total of 5,245 patients treated, 555 (10 per cent) suffered from intercurrent complications and 365 (7 per cent) from reactions due to the arsenicals. These reactions or complications were severe enough to attract notice and interfere with routine treatment.

It is interesting to note that the number of intercurrent complications, ranging from an abscessed tooth to a ruptured appendix, was in considerable excess of the number of reactions to arsenical treatment. In other words, a patient is much more liable to have treatment interfered with by intercurrent complications not caused by the arsenicals than by reactions due to them.

Table 3 gives the type of complications occurring in our clinic, and in parallel columns gives the comparison of the percentage of complications occurring after the administration of arsphenamine and neo-

arsphenamine. This table shows that the incidence of complications was 15 per cent for old arsphenamine and 9 per cent for neoarsphenamine. The principal complications of arsphenamine were those of icterus and disease of the skin and gastro-intestinal tract. Venous and gastro-intestinal symptoms gave little trouble. The patients with icterus were usually hospitalized. For that reason we are unable to say to what extent the kidneys were involved.

There was a slightly higher percentage of nitritoid reactions among the neoarsphenamines. Here, I think, it is desirable to take a little time to give my idea of why we have fewer reactions with neoarsphenamine than with arsphenamine.

TABLE 3.—*Frequency of the Several Types of Reactions Occurring Under Treatment with Arsphenamine and Neoarsphenamine*

Reactions to Arsenical Treatment	Patients Treated with Arsphenamine		Patients Treated with Neoarsphenamine	
	Number	Per Cent	Number	Per Cent
Slight				
Chills and fever	1	0.1	...	....
Gastro-intestinal	11	1.4	...	....
Headache	3	0.4	...	....
Nitritoid	6	0.7	2	1.1
Pruritus	1	0.1	...	....
Cutaneous	15	1.8	2	1.1
Stomatitis	5	0.6	3	1.7
Venous	23	2.8	2	1.1
Total	65	7.9	9	5.0
Severe				
Gastro-intestinal	14	1.7	4	2.2
Cardiac	...	....	1	0.5
Herxheimer	4	0.5	...	....
Icterus	14	1.7	...	....
Renal	9	1.1	1	0.5
Hepatic	1	0.1	1	0.5
Cutaneous	12	1.5	1	0.5
Total	54	6.6	8	4.4
Total number of complications	119	14.5	17	9.4
Total number of cases	819		180	
Total number of cases with complications	108		17	

Last year I said that I had given ten thousand injections of arsphenamine before I had my first case of dermatitis. We then began to give neoarsphenamine in the proportion of six to nine. We gave 0.7 Gm. of arsphenamine and 1 Gm. of neoarsphenamine each week in two doses. With this proportion I had given only a thousand injections of neoarsphenamine before I had three cases of dermatitis in the clinic. I immediately cut down the dose to 0.7 Gm. per week in two doses for each drug, and the comparative results are shown in table 3.

In spite of all this, the reactions have been comparatively few and only moderately severe in the average case. We obtained reactions in 15 per cent of patients given arsphenamine and in only 9 per cent of

those given neoarsphenamine. This, I think, compares favorably with much larger ratios for reactions with neoarsphenamine reported by some of the other clinics. Of course I realize that our group is small and conclusions based on them must be guarded.

Nevertheless there must be an explanation for so great a discrepancy between our results and those reported by other clinics and from private practice. My strong personal opinion is that it is because I have not permitted, from the beginning of the clinic ten years ago, a single dose of neoarsphenamine, silver arsphenamine or arsphenamine to be given in concentration by syringe. Neoarsphenamine and arsphenamine are given in exactly the same dilution and dose and by the gravity method. And I think that our results are a fair recommendation for these precautions. Silver arsphenamine is also given well diluted and by the gravity method.

I am fully aware that there are at least two other factors beside technic which have to be considered as possible causes of reactions. These are idiosyncrasy and a faulty drug.

Idiosyncrasy has decreased in importance as the preparations of arsphenamine have improved in quality. I doubt very much if it would influence materially the percentages of a large number of cases. The manufacturers are to be congratulated on the steady marked improvement and increased safety of their preparations. Yet deterioration may take place after lapse of time, or injury in transit may occur. Tubes of arsphenamine placed close to a hot steam pipe in an express car or on a druggist's shelf would not be improved, to say the least.

The worst reactions that I have had in private practice were from tubes I bought in the open market. Now I go in person to the manufacturer, and have had no trouble since.

It may be helpful to suggest that arsphenamine be packed with the possibility of such accidents in view; also that the manufacturers from time to time test samples from each batch, just as the Army and Navy do with explosives. In this way a deteriorated batch could be recalled before it could do much harm.

COMMENT ON TABLES 4 AND 5

Table 4 indicates that the incidence of complications of treatment is nearly 50 per cent greater among those patients treated with arsphenamine than with neoarsphenamine. Syphilitic patients who began treatment after the disease had reached the latent stage showed a higher percentage of reactions to treatment than those beginning treatment at any other stage. This fact was true regardless of the kind of arsphenamine used (except in the two cases of late secondary manifestations under treatment with neoarsphenamine).

In table 5 the reactions have been classified as severe and slight. Among the patients treated with arsphenamine, the ratio of severe reactions to slight reactions to treatment was 45 to 56 per cent. In the patients treated with neoarsphenamine, the ratio of severe to slight reactions was practically the same—41 to 59 per cent.

TABLE 4.—*Incidence of Complications of Treatment with Arsphenamine or Neoarsphenamine Used as the Predominating Arsenical, According to Diagnosis on Admission*

Diagnosis on Admission	Arsphenamine			Neoarsphenamine		
	Total Number of Cases	Cases of Complications		Total Number of Cases	Cases of Complications	
		Number	Per Cent		Number	Per Cent
Seronegative; primary	30	2	6.7	5	..	....
Seropositive; primary	164	21	12.8	40	3	7.5
Secondary manifestations, first year	323	45	13.9	57	5	8.8
Secondary manifestations, after first year	19	2	0.6	2	1	50.0
Latent	145	24	16.5	42	5	11.9
Tertiary, all later	116	12	10.3	32	3	9.4
Unknown	22	2	9.0	2	..	....
Total	819	108	13.2	180	17	9.4

TABLE 5.—*Incidence of Slight and Severe Complications Resulting from Arsphenamine and Neoarsphenamine, According to Diagnosis on Admission to the Clinic*

Diagnosis on Admission	Complications from Arsphenamine						Complications from Neoarsphenamine					
	Slight		Severe		Total		Slight		Severe		Total	
	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
Seronegative; primary	1	50.0	1	50.0	2	100.0	..	....	..	....	..	.....
Seropositive; primary	13	59.1	9	40.9	22	100.0	2	66.7	1	33.3	3	100.0
Secondary manifestations, fist year	26	54.2	22	45.8	48	100.0	3	60.0	2	40.0	5	100.0
Secondary manifestations, after first year	2	66.7	1	33.3	3	100.0	..	....	1	100.0	1	100.0
Latent	13	48.1	14	51.9	27	100.0	3	60.0	2	40.0	5	100.0
Tertiary, all later	10	66.7	5	33.3	15	100.0	2	66.7	1	33.3	3	100.0
Unknown	1	50.0	1	50.0	2	100.0	..	....	..	....	..	.....
Total	66	55.5	53	44.5	119	100.0	10	58.8	7	41.2	17	100.0

INVESTIGATION OF REPORTS ON DEATHS

Ten years ago no report of so large a number of cases and such a large number of treatments with arsenicals would have been complete without a list of deaths attributable to the treatment.

We have been exceedingly fortunate in having no deaths that could be ascribed to arsenic. Some patients may have died without our knowing it, but we have trailed down every rumor and sent out numerous inquiries, with the result that we have found four patients who died within a short time after the last injection of arsenic in this clinic.

One patient we found had died as a result of an accident, serious enough to have killed him, and there was no question of arsenic poisoning.

Another patient died as a result of carcinoma of the pharynx a month after he left us.

The third one, after receiving three doses of arsphenamine at the clinic, was taken from his home to Bellevue Hospital, where his death was reported and the cause given as dementia paralytica. I have always felt that this might possibly have been a case of hemorrhagic encephalitis, but I have no real data to go by, and must accept the report of Bellevue Hospital.

The fourth patient received 0.25 Gm. of arsphenamine on Monday evening. Friday evening he reported for treatment in perfect health, but when it was discovered that he had eaten a porterhouse steak, he was refused treatment and given a lecture on the subject. The following Monday it was rumored that a patient to whom we had given arsphenamine on Friday had just died in another hospital. Investigation identified the two patients as one and the same. A check-up showed that he had not received any arsphenamine on Friday; that on Saturday, in freezing weather, he had been in the hold of a ship cleaning out a tank, with water up to his knees, and that he had had a chill. The hospital to which he was taken reported that he died of pneumonia.

None of these cases appear among the 999 cases studied, because they had not been under observation for six months or longer.

CONCLUSIONS

I think that it is fairly evident from these statistics and from what has been said that the difference in the efficacy of neoarsphenamine and arsphenamine is not very great when the neoarsphenamine is given well diluted in moderate dosage, and by the gravity method. Certainly the reactions are so much less by the gravity method that this fact should more than counterbalance the convenience of the syringe method. As a matter of fact, considering the high number of reactions reported by other clinics and by physicians in private practice, in which neoarsphenamine is almost universally given by syringe, against the incidence of 9 per cent noted with the gravity method, all the advantages which have been claimed for neoarsphenamine on account of the possibility of giving it with a syringe are absolutely wiped out. As long as physicians insist on giving neoarsphenamine with a syringe, they are looking for trouble, and they will certainly find it.

On the other hand, if they will take the pains to give it well diluted and by the gravity method, they will get nearly as good results as they will with arsphenamine and with fewer complications.

136 West Seventy-Second Street.

ABSTRACT OF DISCUSSION

Dr. Ralph Hopkins, New Orleans: Dr. Thornley asked me to open the discussion on his paper, but as I feel that I have not had sufficient experience to open the discussion on such an important contribution, he has asked some one who really is qualified to do so.

Dr. Clyde L. Cummer, Cleveland: Dr. Thornley's paper, as a careful statistical study of the use of arsenicals in a large clinic, constitutes a valuable contribution to our knowledge of the treatment of syphilis. It is by theaccumulation of such analyses that we are led to certainty as to the best methods to be employed. The important point which the essayist makes is that neoarsphenamine, administered biweekly in conjunction with the intramuscular injections of mercury salicylate, is as efficient in its immediate results as arsphenamine similarly given. This is contrary to common belief, but the conclusion is subject to two reservations, which Dr. Thornley has indicated, namely, (1) that in neither series of cases was spinal puncture possible in a fair proportion and (2) that the number of patients treated by neoarsphenamine is much smaller than that of the patients treated by arsphenamine. Since the question of success in the treatment of syphilis really hinges in large part on the late effects on the central nervous system, one cannot help feeling that final judgment must be suspended until a sufficient number of cases of spinal puncture accumulate.

Dr. Thornley has found, however, that to escape unfavorable complications, neoarsphenamine must be greatly diluted, so that the commonly employed syringe method is not advisable. This being the case, the large clinic might better adhere to the use of arsphenamine, since the greater stability of its solution permits its being made up in large amounts. From the standpoint of the practitioner, who in most cases mixes a single, or at the most, a few doses at a time, there is little choice if in either case he must use large amounts of the diluent by the gravity method.

It is indeed reassuring that in the ten years covered by this study, Dr. Thornley has had no fatalities. Limitation of space prevented his considering the complications more fully, and I hope that he will carry out his intention of publishing later the data on his entire series of 5,000 and more cases, for as he stated, the complications often occur early in treatment. This is an important question because of the widespread use of arsenicals; those who administer them should realize the possibilities and be ever watchful for icterus or the early signs of dermatitis. Occasionally patients are seen in whom arsenicals have been used, with unhappy results, even after the appearance of a rash.

One important point stressed by the essayist was that continuity of treatment has much more to do with its ultimate effect than the total number of injections administered.

Dr. Edward White, Dallas, Texas: To my mind, one statement in Dr. Thornley's paper covered the whole field; that is, when he said to use neoarsphenamine highly diluted. In an experience of about fifteen years with the gravity method, using neoarsphenamine, I have not had the complications and reactions that one reads about in the literature. I think that this is due to the fact that I have always used it well diluted. I know that there are physicians in my town who dilute it in as little as 2 cc. of water and think that they get as good results as if they dilute it well. I doubt that seriously. I think that publication of the single statement that we should give neoarsphenamine well diluted will do more good than we realize, for the slower method is certainly the best.

Dr. J. P. Thornley, New York: We have found that a large amount of neoarsphenamine can be made up quite satisfactorily in a clinic where perhaps two or

three tables are being operated at the same time, as is the case with us. We make up a batch of seven doses at once. That all goes through the apparatus within thirty minutes at the most, so there is no danger, so far as we are concerned, of keeping it in solution too long. Dr. White's remarks regarding the dilution of neoarsphenamine are pertinent. During the past ten years this method has made our work worth while in that we have been remarkably free from the worry of annoying reactions. I feel that what Dr. White has said is of the utmost importance. I believe that the dermatoses and other reactions can be reduced to a minimum if we can induce physicians to dilute well their injections. Then one can have a feeling of safety from unpleasant accidents. The unskilled and careless administration of asphenamine is undoubtedly responsible for many reactions in private practice. I was amused and horrified by a physician of my acquaintance who asked me what caused a severe reaction in one of his cases. A little questioning brought out the fact that he did not have any distilled water handy, so he took water from the tap. He did not say whether he boiled it or not—I hope he did. He mixed the tap water with the neoarsphenamine and gave the injection. The patient had a profound reaction. This physician was not a dermatologist but a general practitioner. I am sure that no one in my audience would think of attempting such a thing.

HYPERGLYCEMIA IN DISEASES OF THE SKIN

ELMORE B. TAUBER, M.D.
CINCINNATI

This paper represents a study of determinations of the blood sugar in over 1,500 persons and of blood sugar tolerance tests made on about half that number. The total series has been divided into three general groups of approximately 500 each.

The first group consists of 514 diabetic patients; the second group, of 504 patients admitted to the medical and surgical services for a great variety of causes; the third group, of 511 dermatologic cases, which are divided into two divisions, division A, 254 cases of various skin diseases which will be summarized later, and division B, 257 cases of furunculosis, pyodermia and ecthyma. It is in the latter group that I was particularly interested, because the generally accepted methods of therapy in these cases caused a personal protest, as in both acute and chronic attacks of boils the traditionally accepted therapy left much to be desired and was seemingly inefficacious for quick relief, and recurrences were the rule rather than the exception. On this account and because so much has been inferred concerning hyperglycemia in skin diseases and furunculosis which seemingly is not correct, I determined to investigate this series of cases in detail and to try to determine what is and what is not so.

It is known that sugar metabolism is regulated partly by the islands of the pancreas and partly by the suprarenal glands, with the assistance of the sympathetic and the parasympathetic nervous system. It is also known that the liver, muscles, fat and skin act as storehouses for the blood sugar. Recently, Zunz added to this knowledge the fact that there exists a central control located in the thalamic or retrothalamic region of the brain, but at present all the factors are not known, so I shall have to give my report from the clinical rather than from the physiologic point of view, which I should have preferred, since an accurate evaluation would be much more valuable than a conjectural one based on clinical evidence. Microchemical methods in facilitating blood sugar tests have made possible a more nearly agreed normal value for blood sugars, and although there still is a divergence of opinion, it is not nearly as wide as it was several years ago. In going over the values given by seventeen authors, the minimum was 64 mg. per hundred cubic centimeters, the maximum,

---

Read before the Fifty-Fifth Annual Meeting of the American Dermatological Association, Havana, Cuba, May 5, 1932.

123 mg., and the average, 90.6 mg.; the value generally accepted is between 90 and 100 mg. The colorimetric method of Folin and Wu was employed in the determinations of the blood sugar, and the interpretation of Hamman and Hirschman was used in the tests for sugar tolerance.

The term blood sugar tolerance test is misleading, since a low tolerance causes a high sugar curve and a high tolerance gives a long flat curve on the graph. In normal persons, within sixty minutes after taking dextrose, the amount rises to from 130 to 180 mg., and this represents the peak of the curve. The blood sugar should return to the normal level within from two to two and one-half hours. The urine of a normal person tested at that time should show no sugar. Poor tolerance is indicated by high peaks and curves which remain high too long or return to normal in a slower manner than is natural; the duration of the curve is possibly a better index of tolerance than the height.

These tests were made at the central laboratory of the Cincinnati General Hospital, under the direction of Dr. S. Dorst and were checked by Miss Christine Vacht, and at the laboratory of the Jewish Hospital under the direction of Dr. M. Herzberg. In addition, studies in about 50 cases were made at four other laboratories, but in the final analysis, the results were all in practical agreement. The cases reported here, approximately 1,500, are from the Cincinnati General Hospital and the clinic of that hospital and the Jewish Hospital and from private practice.

GROUP 1, DIABETIC CASES

In the first group of 514 diabetic patients, 438 were white and 78 Negroes. Determinations of the blood sugar showed a minimum of 162 mg. and a maximum of 444 mg. per hundred cubic centimeters. In most of the patients in this group, the blood sugar and the sugar tolerance peaks were high, and the return to a lower notch was much delayed. Except in a few cases, sugar was usually found in the urine, and the maximum blood sugar was generally reached in two hours and did not fall to the normal level until between the third and fourth hours. The chartograph showed a mean average of 197.4 mg. as the sugar content in this group of cases.

Gangrene and ulcers of the extremities, particularly of the feet, were the most frequent accompaniments of diabetes in the series. The incidence of these and of other complicating conditions are given in table 1, and the age of occurrence in table 2. It is generally believed today that these conditions are not entirely dependent on the diabetic state for their existence. Their occurrence in the nondiabetic persons renders the causative effect of diabetes improbable.

Particular attention has been paid to the incidence of arterial changes, which have been shown usually to be responsible for gangrene. Seventy-seven diabetic patients had arteriosclerosis. A comparison of tables 2 and 3 will show that the greatest number of patients with arteriosclerosis fall in the same age groups as the greatest number of patients having gangrene and ulcers. Similarly, a concurrence of arteriosclerosis and gangrene was noticed in the majority of patients. No patient under 30 years of age in this series was found to have both conditions. Probably long-continued hyperglycemia plays a certain

TABLE 1.—*Incidence of Complicating Diseases in Group 1*

Complication	Number	Percentage
Diabetic gangrene	94	18.0
Diabetic ulcers	22	4.3
Furuncles and carbuncles	18	3.8
Infected hand and feet	12	2.3
Pruritis vulvae et ani	4	0.8
Erysipelas	3	0.6
Epithelioma	2	0.4
Eczema	1	0.2
Psoriasis	1	0.2

TABLE 2.—*Age Incidence of Diabetic Gangrene and Diabetic Ulcer in Group 1*

	Age, Years					
	30-39	40-49	50-59	60-69	70-79	80-89
Diabetic gangrene	2	8	31	32	19	2
Diabetic ulcer	0	6	11	3	2	0

TABLE 3.—*Age Incidence of Arteriosclerosis in Diabetic Persons*

	Age, Years						Total Cases
	20-29	30-39	40-49	50-59	60-69	70-79	
Arteriosclerosis	2	3	10	21	25	15	77

etiologic rôle in the development of arteriosclerosis, which, together with the abnormal metabolic state in diabetes, is responsible for the production of gangrene and ulcers in these patients.

It has been said that furunculosis was a common complication of diabetes before the modern methods of keeping the blood at a normal sugar level were employed. Carbunculosis, tending to involve the posterior cervical and the upper dorsal regions, has similarly been said to have been a frequent complication. In this series, there were only 18 cases of carbuncles and furuncles. The age incidence is given in table 4. A number of other complications have been found in diabetes, as is shown in table 5. Evidently in these cases also the age of predominance of complications lies between 50 and 70.

GROUP 2, MEDICAL AND SURGICAL CASES

The second group comprised 504 patients admitted to the medical and surgical services of the Cincinnati General Hospital and the Jewish Hospital. The values for blood sugar were average, ranging in general from a minimum of 79 mg. to a maximum of 145 mg., with a mean of

TABLE 4.—*Age Incidence in Occurrence of Carbuncles and Furuncles in Group 1*

	Age, Years						Total Cases
	10-19	20-29	30-39	40-49	50-59	60-69	
Carbuncles and furuncles.....	1	1	3	3	5	5	18

TABLE 5.—*Age Incidence of Other Complicating Conditions in Diabetes*

	Age, Years							Total Cases
	10-19	20-29	30-39	40-49	50-59	60-69	70-79	
Infected hands and feet.....	0	0	0	1	8	2	0	12
Cellulitis.....	1	0	0	0	2	4	1	8
Pruritis vulvae and ani.....	0	1	1	0	1	1	0	4
Erysipelas.....	0	0	0	0	1	1	1	3

TABLE 6.—*Incidence of Diseases in Group 2*

Respiratory diseases			**Fractures**	31	88
Bronchitis	16		Accidents	53	
Asthma	11				
Pneumonia	12	52			
Pleurisy	5				
Tuberculosis	8		**Surgical operations**		
Urinary diseases			Gallbladder	21	
Prostatic disease	27		Appendix	50	
Uremia	11		Brain	4	106
Nephritis	32	99	Kidney	4	
Cystitis	14		Prostate	17	
Malignant conditions	15				
Cardiac diseases			**Miscellaneous cases**		
Myocarditis	11		Thyroid	5	
Valvular disease	31	75	Otitis media	4	
Arteriosclerosis	33		Anemia	7	
Intestinal diseases			Nervous diseases	9	
Malignant conditions	5	9	Under observation	4	62
Duodenal disease	4		Glandular dysfunction	11	
Hepatic diseases			Lead and mercury poisoning	5	
Malignant conditions	11	13	Miscellaneous	17	
Abscess	2				

111.4 mg., and the sugar tolerance was low, with a return to normal in two hours or even less. There were 299 white persons and 205 Negroes in this group suffering from a range of diseases.

The cases were divided into groups, as is shown in table 6. In this group also the arterial changes fall in the same age groups as do the greatest number of persons having gangrene and trophoneurosis, and similar conditions.

In the group of cases shown in table 7, with a normal or lowered sugar content, there were 39 cases of furuncles and carbuncles, or more than twice the number found in the diabetic group; here also there was an incidence of infected hands and feet and of cellulitis in 43 cases, or over double the number occurring in the diabetic group.

GROUP 3, DERMATOLOGIC CASES

The third group was to me of the most interest, as it comprised 511 dermatologic cases. These were divided into two divisions. In

TABLE 7.—*Incidence of Diseases in the Nondiabetic Group 2*

Diseases	Number	Percentage	Age, Years 30-39	40-49	50-59	60-69	70-79
Respiratory	52	9.6	6	11	17	15	3
Urinary	99	19.3	5	12	23	21	38
Cardiac	75	13.4	4	9	15	20	27
Intestinal	9	2.1	..	1	2	2	4
In other organs	13	3.0	1	2	4	3	3
Accidents	88	18.0	19	22	6	11	30
Operations	106	22.0	31	21	14	19	21
Miscellaneous	62	12.5	8	11	13	21	9

TABLE 8.—*Incidence of Diseases in Group 3, Division A* *

Diseases	Number	Percentage	Range of Blood Sugar Values, Mg.	Age Incidence, Years 30-39	40-49	50-59	60-69	70-79
Seborrheic dermatitis	15	5.8	82-108	4	2	1	3	5
Burns	24	9.4	88-100	..	..	..	..	..
Prurigo	2	0.9	91- 93	1	..	1	..	..
Syphilis	27	10.3	85-104	6	7	5	6	3
Scabies	28	10.6	90-117	7	5	5	6	5
Eczema	47	19.6	93-119	4	7	11	18	7
Mycosis fungoides	2	0.9	91- 95	1	..	..	..	1
Psoriasis	14	5.6	94-118	2	3	3	4	2
Lichen planus	11	4.3	84-103	1	1	2	3	4
Erythemas	14	5.7	86-110	2	3	2	3	4
Tineas	35	14.4	87-111	6	7	4	9	9
Urticaria	8	3.1	92-105	2	2	1	3	0
Acne	12	3.6	94-117	11	1	0	0	0
Tuberculosis of the skin	15	5.8	90-106	2	5	4	4	0

* Sugar tolerance and return to normal occurred in practically all patients within the two and one-half hour limit.

division A of 254 cases of various dermatoses, 189 occurred in white patients and 65 in Negroes. In this group the values for the blood sugar were average, ranging in general from a minimum of 80 mg. to a maximum of 119 mg. with an average of 102.4 mg. In division B the minimum blood sugar value was 82 mg., the maximum, 111 mg. and the average 97.6 mg. The incidence of diseases in division A and in division B are shown in tables 8 and 9, respectively.

In division A, no glycemic curves occurred in seborrheic eczema, furunculosis and other pyodermias, dermatitis venenata, scabies, lupus, tineas and burns. In these diseases, presumably there is no disorder

of carbohydrate metabolism, although single instances may show curves altered in a glycemic state. In acne, psoriasis and eczema, there is no general hyperglycemia, but cases are found in which glycemia exists.

TABLE 9.—*Incidence of Diseases in Group 3, Division 6* *

Diseases	Number	Range of Blood Sugar Values, Mg.	Percentage	Age Incidence, Years 20-29	30-39	40-49	50-59	60-69	70-79
Furunculosis (localized)	217	82- 96	84.6	56	44	38	30	29	20
Ecthyma	19	86-105	7.6	2	3	5	3	6	0
Pyodermia (generalized)	21	84-111	7.8	7	2	2	4	5	1

* Sugar tolerance of all patients returned to normal in less than two and one-half hours.

TABLE 10.—*Wenckebach Diets*

Foods	Weight	Protein	Fat	Carbohydrate	Calories
Breakfast:					
15% fruit	200	2.00	....	28.00	120
Cornflakes	30	2.40	0.15	25.95	116
Whole milk	200	6.50	3.00	10.00	138
Sugar	20	....	....	20.00	30
Egg	50	6.70	5.20	.....	74
Bread	80	7.44	0.96	41.76	206
Butter	10	0.10	8.50	.....	77
Cream	30	0.80	6.60	0.80	66
Coffee					
		26.04	29.41	126.51	877
Dinner:					
Liver	45	8.87	3.60	.....	68
Potato	150	3.30	0.15	27.00	123
10% vegetable	150	1.50	....	15.00	66
10% vegetable	150	1.50	....	15.00	66
Bread	80	7.44	0.96	41.76	206
Butter	15	0.15	12.75	.....	115
10% fruit	190	1.90	....	19.00	84
Whole milk	200	6.60	8.00	10.00	138
Lactose	50	....	....	50.00	200
		31.26	25.46	177.76	1,066
Supper:					
Rice	150	2.70	0.15	31.95	140
10% vegetable	150	1.50	....	15.00	66
10% vegetable	150	1.50	....	15.00	66
Salad					
5% vegetable	80	0.80	....	4.00	19
Mayonnaise	10	0.13	8.38	.....	76
Bread	80	7.44	0.96	41.76	206
Butter	10	0.10	8.50	.....	77
15% fruit	200	2.00	....	28.00	120
Whole milk	200	6.60	8.00	10.00	138
Lactose	50	....	....	50.00	200
		22.77	25.99	195.71	1,108
		80.07	80.36	499.98	3,051

Protein, 80; fat, 80; carbohydrate, 500; calories, 3,040 (from 3 to 6 weeks)

Such cases are exceptional and repeated tests of the sugar tolerance are required.

These amazing figures, together with a dissatisfaction with the results of the present therapy in furunculosis, prompted me to employ other methods of treatment in the last group. In a series of 189 cases

of furunculosis, the following method was employed, with a striking response, both subjectively and objectively: Locally, wet dressings of physiologic solution of sodium chloride or a weak Burow's solution were applied. I was unable to find or demonstrate a high blood sugar content in these cases of furunculosis, and I reasoned that perhaps the lowered resistance of the constitution to the pyogenic organisms that invade the system may be due to a lack of carbohydrates and sugars; so all patients were given a very high carbohydrate diet (Wenckebach no. 3) plus feedings of liver extract.

Intravenous injections of 500 cc. of 5 per cent dextrose were given daily for six successive days. The results were astonishing, as the patient in almost every instance volunteered the information that the feeling of pain and tension lessened after the second injection, while objectively the signs of inflammation diminished and in 50 per cent of the cases did not progress to suppuration and sloughing of necrotized tissues, but absorbed slowly, although there was an induration at the site of injection, owing to the attempts of the tissues to wall off the inflammation. Another striking occurrence was that there were only 4 cases of recurrence of a second boil and only 1 in which there was a third furuncle. This, to me, seems a direct proof that the antibodies necessary for resistance to the invasion of pus formers are provided by the dextrose and an increased intake of starch. This, of course, will require careful checking and investigation and corroboration by other investigators, and a like finding by them.

SUMMARY

In summarizing, I wish to state that, in direct opposition to the statements in the literature that common disorders of the skin are associated with hyperglycemia, I find that almost without exception the blood sugar is normal, and that in furunculosis the reverse of hyperglycemia is the rule and the fact.

Whether or not certain groups of cutaneous diseases are connected regularly with hyperglycemia is doubtful.

I believe that dextrose given intravenously, combined with a high carbohydrate diet, is almost a specific in the cure of furunculosis.

ABSTRACT OF DISCUSSION

DR. WALTER J. HIGHMAN, New York: The first paper that I read before this body was written in collaboration with Dr. Schwartz and was on the same subject as the present paper. Our finding was of hyperglycemia suspected if not actually to be found in cases of the following groups: folliculitis, acne and the pyodermias. Our figures for blood sugar ranged from normal to high points. At the same meeting, Dr. Gilchrist and Dr. Pels presented a similar report in which they found that in the group in which we had found hyperglycemia, they had not done

so. This was a *casus belli* for several years. I think it was several years ago that Dr. McGlasson published a paper stating that he found hyperglycemia in eczema. Now Dr. Tauber presents a group of cases indicating that hyperglycemia in dermatologic conditions is unimportant and inconstant.

Certainly there has been nothing in the past to indicate any causal relationship between hyperglycemia and cutaneous lesions. As a matter of fact, an interesting way of approaching the question of the relationship of dermatoses to findings in the domain of chemistry is to examine the patients in a hospital, as I have done, to see how many cutaneous lesions can be found in patients with diabetes and other metabolic diseases. One will be surprised to find how large a percentage of such patients have no dermatoses. I have always been very skeptical about the meaning of laboratory statistics applied at random to various dermatoses. I certainly believe that I misled myself in my previous work, but I am clearly convinced that I misled nobody else.

Dr. William Allen Pusey, Chicago: I am extremely shy about coming to any conclusion concerning the question discussed, but I have been impressed with the fact that sugar has for hundreds of years been incriminated in dermatoses, without any practical ground, and I hope to accept Dr. Tauber's findings. Of course, this question will require further investigation.

Dr. Samuel Sweitzer, Minneapolis: It is interesting that Dr. O'Brien told me that in checking over a good many thousands of cases of diabetes at the University he found that death was due to pyogenic infection in a vast majority, this infection often occurring in the feet from cutting the nails, etc.

Dr. E. B. Tauber, Cincinnati: I was afraid that there might be an entire disagreement on this subject, and I only hope that sixteen years from now I will not have to apologize for this presentation. I agree with Dr. Pusey that it will require many investigations by many investigators, with uniform results, before the work will be proved of value.

INTRADERMAL AND CUTANEOUS METHODS OF TESTING IN FOOD ALLERGY

A COMPARATIVE STUDY

JOSEPH T. BELGRADE, M.D.
WHEELING, W. VA.

Allergy is an altered reactivity of the body cells to an exciting substance which is harmless in similar amounts for the majority of members of the same species. This exciting substance, or allergen, may or may not be primarily a foreign protein. Among the proteins capable of playing the rôle of allergen are the pollens, foods, serums, animal emanations, products of bacteria and fungi and animal parasites. Of these, the pollens and foods hold the greatest clinical importance.

Foods, proportionately, play a much greater rôle than pollens in the production of allergic symptoms, since people are more likely to become sensitized to substances with which they come in contact most frequently. The offending foods are usually the common ones, such as milk, wheat and eggs, and also the foods eaten in the greatest quantity. Various clinical conditions, such as asthma, eczema, angioneurotic edema, urticaria and the erythemas, are now definitely recognized as manifestations of hypersensitiveness to foodstuffs.

Allergy first received its proper recognition in 1913. Schloss [1] and Cooke,[2] working independently, reported methods by which sensitiveness to various proteins could be determined by cutaneous reactions. With the introduction of definite diagnostic procedures, allergy has had widespread clinical appreciation.

Since 1913, the appreciation and importance of the condition now known as allergy have greatly increased. In looking back over the medical literature, one finds occasional instances reported of unexplained and peculiar reactions to many different substances, the nature of which now can be termed allergic. Indeed, a great many reactions, such as

---

Dr. Jay F. Schamberg assisted in this study by outlining the work. These studies were carried out in the offices of Dr. Schamberg and Dr. Carroll S. Wright.

Abridgment of a thesis accepted by the faculty of Dermatology-Syphilology of the Graduate School of Medicine of the University of Pennsylvania, in partial fulfilment of the requirements for the degree of Master of Medical Science for graduate work in dermatology-syphilology.

1. Schloss, O. M.: A Case of Allergy to Common Foods, Am. J. Dis. Child. **3**:341 (June) 1912.

2. Cooke, R. A.: The Treatment of Hay Fever by Active Immunization, Laryngoscope **25**:108, 1915.

those of infants and children to milk, eggs and cereals, were well known to the laity, but occupied no place in medical literature. Peculiar eruptions due to drugs were well recognized, but they were not identified as allergies until 1916, when Cooke [3] noticed the relatively large number of such cases occurring among hypersensitive persons, and remarked the similarity of symptoms of reactions to drugs to those due to foreign proteins in specifically hypersensitive persons.

The skin plays an important rôle in the mechanism of recovery from disease of the internal organs by destroying bacteria and toxic products during the process of elimination. It is highly probable, owing to this important function of elimination, that the skin may become sensitized or allergic by nature of the intimate part it plays during the course of disease.

The history of the patient may not reveal the cause or it may be misleading. By this procedure alone it is difficult to arrive at a diagnosis of the exciting substance that produced the symptoms. In many instances the patient may say that he has frequently partaken of a certain food or foods without disturbance. An apparent explanation, according to Pollitzer,[4] is that the harmful substance may have passed through the alimentary canal many times without producing symptoms, but that once, through some accidental circumstance, it passed more or less unchanged through the intestinal walls into the blood stream. The seat of the disturbance, therefore, is the presence of the exciting substance not in the alimentary canal, but in the cells of the skin which have been sensitized by previous contacts with the substance through the circulating blood. As a consequence an antibody is now formed, which remains fixed in or on the cells, capable of producing an intracellular reaction when the corresponding allergen or exciting substance is introduced. The main lesion of such reactions is a wheal, due to vasomotor paralysis, characterized by dilatation of blood vessels and serous exudation. This antibody-allergen phenomenon is a true allergic reaction and is highly specific.

In food allergy, reactions may be elicited by the absorption of the exciting substance from the gastro-intestinal tract. Likewise, local and systemic reactions may be elicited by the application of these substances to abrasions of the skin or by intradermal injections. The amounts of allergens necessarily required to elicit cutaneous reactions are infinitely small.

The allergic skin reaction, therefore, is considered highly specific and constitutes the most valuable single aid in the diagnosis of food

3. Cooke, R. A.: The Cutaneous Reactions: The Dangers of the Diagnostic Cutaneous Test and Therapeutic Injection Method, J. Immunol. **7**:119, 1922.

4. Pollitzer, Sigmund: Allergy in Skin Diseases, Bull. New York Acad. Med. **5**:232, 1929.

allergy. Two of the principal methods of testing the skin are the cutaneous or scratch method and the intradermal or injection method. As has been stated, the patient's own observation may be erroneous or untrustworthy, and resort must be had to sensitization tests. Such being the case, the approach toward establishing an immediate diagnosis is by the cutaneous reaction, as determined by one of two methods. In order to obtain the best results, therefore, one should know the relative value of each of these methods.

REVIEW OF THE LITERATURE

The first report on experimental observation of cutaneous sensitiveness in allergy was published in 1873 by Blackley,[5] a surgeon of Manchester, England. He demonstrated the causal relationship of the pollens to seasonal hay fever. His work was based not on general observations alone, but on many and laboriously carried out experiments. Blackley tested patients with pollens by various methods, one of which was by inoculating fresh, moistened pollen into the upper and lower limbs. This procedure immediately caused a local reaction characterized by intense itching and edema at the site of the inoculation.

Even though Blackley demonstrated that a cutaneous test could be diagnostic of sensitiveness to pollen, it took almost fifty years to develop satisfactory methods to make this discovery practical. Diagnostic efforts were entirely limited to the pollens until within the past few decades, when common foods came under suspicion as possible causes of many varied and unusual symptoms. The first description to appear in the literature was in 1909, when Smith [6] reported his classic case of buckwheat poisoning, proving that foods could cause allergic symptoms. The history of the patient suggested buckwheat as the exciting cause. Smith rubbed into a scarified area on the left arm a minute drop of a sterilized infusion of the cereal, and within fifteen minutes after the vaccination, the patient complained of a "tight feeling" in his chest and nausea in the "pit of the stomach," followed by asthmatic breath sounds, marked urticaria and edema of the lips. In addition to these systemic symptoms, the scarified area of the left arm presented a large urticarial wheal. The general symptoms subsided one-half hour after their onset. The local reaction disappeared several hours later. The control test, with a mixture of sterile flour and water, was negative. Smith's report well illustrates what an important rôle foods may play in allergy. It also shows that this hypersensitiveness or allergy is a highly specific phe-

5. Blackley, C. H.: Experimental Researches on Cause and Nature of Catarrhus Aestivus, London, Baillière, Tindall & Cox, 1873.

6. Smith, H. L.: Buckwheat-Poisoning: Report of a Case in Man, Arch. Int. Med. **3**:350 (May) 1909.

nomenon, and that the degree of sensitiveness favorably compares with that of the local and systemic reactions.

Schmidt,[7] in 1910, performed a series of experiments on children of different ages. He made cutaneous tests with puro, a preparation that consists of egg white, beef, glycerin and salts. He reported a positive reaction as an area of redness or a raised papule (wheal), which appeared from eight to twenty-four hours after the inoculation, and observed that the positive reactions increased with time. In his investigation, he employed the scratch method. The reactions he observed reached the highest intensity after from eight to twenty-four hours. These reactions are quite different from those obtained in food allergy, which, with the Pirquet technic, usually reach their greatest height within one hour.

In order to avoid dangerous anaphylactic reactions, Moss [8] in 1910 advocated a preliminary intradermal test before the injection of antitoxic serum, especially for those who had previously received horse serum. He injected intradermally 0.01 cc. of undiluted horse serum into the inner side of the upper part of the arm. According to his report, an erythema of from 1 to 2 cm. in diameter, which appeared within twenty-four hours and disappeared within from two to three days, constituted a positive reaction. More pronounced local manifestations occurred in those who had had a previous antitoxic serum injection. These persons gave a sudden and violent reaction at the site of the inoculation, marked by the prompt appearance of an urticarial wheal about 1.5 cm. in diameter surrounded by an areola of inflammation about 5 to 6 cm. in diameter. In addition, marked itching accompanied the appearance of the local reaction.

Moss received little recognition for his investigation, and his intradermal technic did not become generally known or adopted, since he limited his work solely to determine in advance probable anaphylactic reactions, which occasionally occur with the second injection of antitoxic serum. Also, these local reactions appeared within twenty-four hours after the injections, which is a considerable interval as compared with the immediate reactions (from five to thirty minutes) seen in the pollen and food allergies.

Schloss,[1] in 1912, reported the first successful attempt to make diagnostic use of skin reactivity in a case of allergy to eggs, oatmeal and almonds. He employed cutaneous inoculations on the principle of Pirquet's tuberculin test. The Pirquet "borer" was used as a scarifier to produce a uniform abrasion of the skin, into which the substance to

7. Schmidt, H.: Beiträge zum Studium der cutanem Allergen, Arch. f. Kinderh. **53**:349, 1910.

8. Moss, W. L.: A Cutaneous Anaphylactic Reaction as a Contra-Indication to the Administration of Antitoxin, J. A. M. A. **55**:776 (Aug. 27) 1910.

be tested was gently rubbed. The active substances produced a distinct urticarial wheal surrounded with erythema at the site of inoculation. The reaction appeared from ten to thirty minutes after the test was made. By employing proper control tests, Schloss ascertained that the cutaneous reaction was not the result of chemical or mechanical irritation, but was caused only by certain food substances and "to a marked degree only in those to which the patient had exhibited a pronounced idiosyncrasy."

In 1914, Talbot [9] commented on the "brilliant investigations" of Schloss. This author applied the cutaneous test according to Schloss on eleven patients suffering from eczema and asthma who were sensitive to eggs. These cases were studied to determine, by means of the reaction to the scratch test, any possible connection between eggs in the food and asthma.

Goodale,[10] in 1916, and Walker,[11] in 1917, independently reported the following: "It has been known for some years that an individual sensitive to a given proteid may exhibit a characteristic reaction if the proteid is brought in a soluble form in sufficient concentration into contact with a scratch in the skin." Goodale regarded the application of skin tests as an important diagnostic procedure. Walker employed the skin tests according to the Schloss technic until 1916, when the material applied in the test was in the form of a powder which represented the dry residue of an extract of the original material.

First to use allergens intradermally for the purpose of diagnosis was Robert A. Cooke,[2] who began his allergic investigations in 1911. Cooke devoted his attention to the treatment of hay fever by active desensitization, employing solutions of the pollen protein. This liquid preparation was most conveniently given by subcutaneous injection. In order to determine the specific factor or factors in any allergic person, it was convenient also to use these liquid preparations for intradermal skin tests. Cooke found these tests of great diagnostic importance, because when a solution of pollen protein was injected intradermally (from 0.01 to 0.05 cc.), a typical local reaction occurred within from ten to thirty minutes at the site of the injection only in the persons sensitized to that protein. This method was adopted and employed by Cooke and his associates to determine the specific pollen before instituting the desensitization treatment by injection.

---

9. Talbot, F. B.: Asthma in Children: Its Relation to "Egg Poisoning," Boston M. & S. J. **171**:708, 1914.

10. Goodale, J. L.: The Diagnosis and Management of Vasomotor Disturbances of the Upper Air Passages, Boston M. & S. J. **175**:181, 1916.

11. Walker, I. C.: Studies of Sensitization of Patients with Bronchial Asthma to Bacterial Proteins as Demonstrated by the Skin Reaction and the Methods Employed in the Preparation of These Proteins, J. M. Research **35**:487, 1917.

Owing to the reports of Schloss and Cooke on different diagnostic methods of skin testing, investigators began to check up on the merits of each of these methods. Blackfan,[12] in 1916, found the intracutaneous test more delicate than the cutaneous. He conducted a series of comparative tests on forty-three persons who gave a negative history to eczema, asthma and idiosyncrasy to foods. In this series, only one of the entire group gave a positive reaction. This reaction occurred with the intradermal method. Later, he tested twenty-seven patients with eczema. The scratch test was made on all, of whom thirteen gave a positive reaction. Nineteen patients were tested intradermally, and of these, seventeen gave positive reactions to one or more food substances. Eleven of the fourteen patients who gave a negative reaction with the cutaneous method were tested intradermally, and a positive reaction was obtained in nine. In two patients the reaction was negative with both methods.

This investigation was soon followed by others. Walker and Adkinson,[13] in 1917, reported on a series of twenty-two selected patients sensitive to various pollens. A comparative study was made. With the intradermal method, they injected 0.1 cc. of the pollen solution, which is at least from five to ten times the volume necessary. As one would expect, such large injections mechanically produced larger wheals and more pronounced local and systemic reactions. These investigators incidentally were misled in their findings, stating that the intradermal test was "much too sensitive," less specific and more difficult to perform, whereas the cutaneous test was specific, sufficiently active and easy to give.

Schloss,[14] in 1920, investigated the relative value of his test to that of Cooke. He conducted a series of comparative tests. In his report, Schloss expressed the opinion that the intradermal method was more sensitive, in many cases producing positive reactions while the cutaneous tests gave negative ones in persons known to have a mild protein idiosyncrasy. At that time he thought that the intradermal test was "apt to be misleading," owing to the pseudoreactions that frequently occurred. He also reported two cases in which severe infection followed this test.

In a series of seventy-eight patients clinically sensitive to proteins, Brown,[15] in 1922, conducted his comparative investigations and found

12. Blackfan, K. D.: Cutaneous Reactions from Proteins in Eczema, Am. J. Dis. Child. **11**:441 (June) 1916.

13. Walker, I. C., and Adkinson, J.: A Comparison Between the Cutaneous and the Intradermal Tests in the Sensitization of Asthmatic and Hay Fever Patients, J. M. Research **37**:287, 1917.

14. Schloss, O. M.: Allergy in Infants and Children, Am. J. Dis. Child. **19**:433 (June) 1920.

15. Brown, Aaron: The Diagnostic Cutaneous Reaction in Allergy: Comparison of the Intradermal Method (Cooke) and the Scratch Method (Schloss), J. Immunol. **7**:97 (March) 1922.

the intradermal test superior to the cutaneous. In his series he obtained positive reactions in all with the intradermal test and in only 50 per cent with the dry commercial preparations. In making the intradermal test, he injected 0.01 cc. of the solution, instead of 0.1 cc., thereby obtaining sufficiently sensitive and more specific reactions. His results, therefore, were quite different from those reported by Walker and Adkinson. In a later publication based on his experiment, Brown [16] stated that "there can be no question that the intradermal method used by Cooke and his school is by far the most accurate."

In that same year, Larsen, Paddock and Alexander [17] studied the comparative results in a series of fifteen persons sensitive to protein. These investigators believe that more cutaneous tests can be done at the same sitting, with less time and trouble. Their clinical results, however, showed that the alleged technical advantages of the scratch method were outweighed by the increased reliability of the intradermal method. In their series of fifteen subjects there was no definite response to the dry commercial allergens applied by the scarification method, although the history and intracutaneous tests were positive. In no case was the scratch test positive and the intradermal negative.

Ramirez and Eller [18] investigated the diagnostic value of various methods in a large series of sensitization tests. Their findings were in accord with those of others in that the intradermal method was more sensitive, but more apt to produce false reactions as well as alarming systemic symptoms in hypersensitive persons.

An interesting case of dermatitis due to lettuce was recently reported (1932) by Rinkel and Balyeat,[19] which clearly reveals the relative value of various methods of making skin tests as a distinct aid in the diagnosis of protein sensitization. The patient, a woman 43 years of age, a salad maker who had handled large amounts of lettuce over a period of five years, was subject to urticarial eruptions. Only the exposed parts were affected, such as the hands, forearms, face and neck. When first tested, she gave a negative reaction to the scratch test and a positive reaction to the contact or patch test to lettuce. A clinical cure was effected by eliminating lettuce from her diet and occupation. At this time, the cutaneous test was repeated, and the intradermal method was also employed. She gave negative reactions to both scratch and patch tests.

16. Brown, Aaron: Present Day Treatment of Asthma, M. J. & Rec. **118**:333 (Sept. 19) 1923.

17. Larsen, N. P.; Paddock, R., and Alexander, H. L.: Bronchial Asthma and Allied Conditions, J. Immunol. **7**:81 (March) 1922.

18. Ramirez, M. A., and Eller, J. J.: Intradermal, Scratch, Indirect and Contact Tests in Dermatology, J. A. M. A. **95**:1080 (Oct. 11) 1930.

19. Rinkel, H. J., and Balyeat, R. M.: Occupational Dermatitis Due to Lettuce, J. A. M. A. **98**:137 (Jan. 9) 1932.

but a positive reaction to the intradermal test. This shows that the intradermal method is more delicate and reliable.

The introduction of the two allergic skin test methods, as proposed by Schloss and Cooke, marked the beginning of an extensive investigation of the question as to which method of testing to employ from the standpoint of superiority and reliability. Owing to the difference in the technic, the tendency has been to employ one method to the exclusion of the other. Cooke [2] and others who adhere to the intradermal method claim it to be more delicate and more sensitive than the cutaneous test of Pirquet. They also point out that the Schick test by the intradermal route is more reliable and practical than when it is done by the scratch method. Peshkin and Fineman [20] expressed the belief that the whole problem involves the degree of concentration of the test material employed. In their study, the question was which method with the test materials at hand was more reliable and best suited for each protein employed. These investigators, owing to the fact that the dry powders that they used were more concentrated and more potent than the dry allergens furnished by commercial houses, claim that from the standpoint of diagnosis and safety the scratch method appeared to be superior to the intradermal as a routine procedure for testing. Their claim substantiates that of previous workers, who concluded that the intradermal test was erratic. Unger,[21] in 1928, expressed the opinion that the intracutaneous is not more satisfactory than the cutaneous test and that in most instances when one is negative, the other is also. Others have reported opposite results. Blackfan,[12] in his comparative study, found the intradermal tests more delicate than the cutaneous. Kern [22] in 1927 remarked that the cutaneous scratch tests are apt to be negative to pollens, to animal emanations and especially to active food allergy. Ramirez and Eller [18] felt that the intradermal is a distinctly more valuable test in spite of the fact that it is more apt to produce occasional false local reactions. Schloss,[14] Brown [15] and Larson, Paddock and Alexander [17] concurred in this opinion. Criep,[23] in a recent publication, remarked that the scratch method is simple and safe and yields fairly good results, while with the intradermal method the results are more reliable and clearcut. Rowe,[24] a noted investigator of food allergy, com-

20. Peshkin, M. M., and Fineman, A. H.: A Comparative Study of the Scratch and Intradermal Methods of Skin Testing, Am. J. Dis. Child. **34**:815 (Nov.) 1927.

21. Unger, Leon, in discussion on Rowe, A. H.: Food Allergy: Its Manifestations, Diagnosis and Treatment, J. A. M. A. **91**:1623 (Nov. 24) 1928.

22. Kern, R. A.: The Interpretation of Skin Tests, Atlantic M. J. **30**:290 (Feb.) 1927.

23. Criep, L. H.: The Allergic Factor in Dermatology, Pennsylvania M. J. **35**:78 (Nov.) 1931.

24. Rowe, A. H.: Food Allergy: Its Manifestations, Diagnosis and Treatment, J. A. M. A. **91**:1623 (Nov. 24) 1928.

menting on the comparative value of both methods, stated that the frequency with which the scratch test fails to show definite food allergy should be emphasized because of the common use of this method by physicians, and that the intracutaneous test, with food extracts made by Coca's [25] method, has been used in many patients having negative reactions to the scratch test with frequent positive reactions. Kolmer [26] claimed that the intradermal method is more delicate, but is likewise subject to error in interpretation.

EXPERIMENTAL DATA

The following report is based on a comparative study of the intradermal and scratch methods as applied to a series of fifty patients with allergic dermatoses as they presented themselves at the office of Dr. Jay F. Schamberg. Both tests were done simultaneously. The commercial dry powder allergens were employed in performing the scratch tests, and the liquid allergens, obtained from the Research Institute of Cutaneous Medicine and prepared after the method described by Coca,[25] were employed in performing the intradermal tests.

Technic.—Scratch Test: Depending on the number of tests to be made, the skin of the arm, forearm or both is cleansed with alcohol and dried. In young infants the back is preferable. A series of abrasions are made on the inner side of the flexor surface of the arm. As a scarifier, the Pirquet "borer" should be used, since it produces a uniform abrasion about ⅛ inch (0.3 cm.) in diameter. The scratch must be deep enough to reach through the dead skin to the superficial lymphatics, but not deep enough to draw blood. A slight oozing of serum is desirable. The dry allergen should be placed on the scratch with a sterile wooden applicator or toothpick, then moistened with tenth-normal sodium hydroxide solution, which is applied with the opposite end of the same applicator and rubbed thoroughly into the scratch. A new applicator is used for each substance to be tested. The abrasions should be 2 inches (5 cm.) apart, in order that the positive reactions may be clearly defined. The control test receives a drop of the hydroxide solution, followed by the same amount of rubbing in exactly the same manner, except that no protein is used. One-half hour later the proteins are washed off, and the results noted. In subjects who are not too hypersensitive, the immediate reading is made at the end of one hour.

Intradermal Test: Aseptic precautions are employed as with the scratch test. The skin of the outer side of the flexor surface of the arm is selected, and the injections are made opposite to those already made with the scratch test (for comparative study of the two methods). Each injection should be at least 2 inches apart and also 2 inches away from the corresponding scratch test. The control test, which is made by the intradermal injection of a physiologic solution of

25. Coca, A. F.: Studies in Specific Hypersensitiveness: The Preparation of the Fluid Extracts and Solutions for Use in the Diagnosis and Treatment of the Allergies with Notes on the Collection of Pollens, J. Immunol. **7**:163 (March) 1922.

26. Kolmer, J. A.: Infection, Immunity and Biologic Therapy, ed. 3, Philadelphia, W. B. Saunders Company, 1925, p. 682.

sodium chloride, is made opposite the scratch control, also 2 inches apart. In the performance of the intradermal test a graduate tuberculin syringe, fitted with a fine no. 26 platinum-iridium needle, should be employed. The syringe and needle are thoroughly sterilized before and thoroughly cleansed in sterile distilled water for each protein. The allergen is injected intradermally and not subcutaneously, because of the danger of systemic reactions that have occurred in very sensitive patients. The needle is entered eye upward until the eye is completely in the epidermal layer. From 0.01 to 0.02 cc. of allergen is injected, which produces a white elevated blanched area. If this wheal formation is not seen, the injection is too deep, and the test is apt to be unsatisfatory. The amount of protein injected should not exceed 0.02 cc. This precaution lessens the amount of pain, reduces the degree of trauma and minimizes the occurrence of pseudopositive reactions.

Reaction.—When the results are read, the control test is inspected and is to be compared with the protein reactions. A distinct wheal surrounded by an area of erythema in the presence of a negative control test indicates a positive reaction. The wheal should be irregular in outline, and the edges should never be sharply defined. This irregularity is due to edema spreading along the lymph spaces, and is likened to the pseudopodia of the ameba. Such a reaction is interpreted as an allergic expression in the skin (Schamberg [27]). The immediate positive reactions occur within a few minutes with the intradermal test (not later than twenty minutes) and with the cutaneous test within from ten to thirty minutes. As a rule, positive reactions persist from one to twenty-four hours. The traumatic and the nonspecific protein reactions disappear within that time, thereby permitting more accurate readings.

A doubtful reaction consists of a small area of erythema, measuring 0.5 cm. in diameter, in the presence of a negative control test. This reaction may be considered doubtful or weakly positive and should be repeated at a later date. Cooke [28] has divided the skin reaction into three groups: immediate, delayed and negative reactions. The immediate reactions are classified as marked, moderate or slight, and are designated as 3 plus, 2 plus and 1 plus, respectively. The markedly positive is the only reaction showing pseudopod projections. This classification, no doubt, may be satisfactory for practical purposes, but Peshkin and Fineman [20] believe that the size of the various skin reactions must be definitely stated, as follows:

1. A 1 plus, or slightly positive, reaction is an urticarial wheal from 0.5 to 1 cm. in diameter with a surrounding zone of erythema.

2. A 2 plus, or moderately positive, reaction is an urticarial wheal from 1 to 2 cm. in diameter with a surrounding zone of erythema.

3. A 3 plus, or markedly positive, reaction is an urticarial wheal more than 1 cm. in diameter with pseudopod projections and a surrounding zone of erythema.

4. A reaction measuring less than the foregoing and more than the control with little or no surrounding zone of erythema is a plus-minus reaction.

5. Delayed reaction consists of a zone of erythema at the site of the inoculation, resembling somewhat a beginning infection.

6. A negative reaction with either method of skin testing does not differ in any way from the control test.

---

27. Schamberg, J. F., in discussion on Bloch, Bruno: The Rôle of Idiosyncrasy and Allergy in Dermatology, Arch. Dermat. & Syph. **19**:220 (Feb.) 1929.

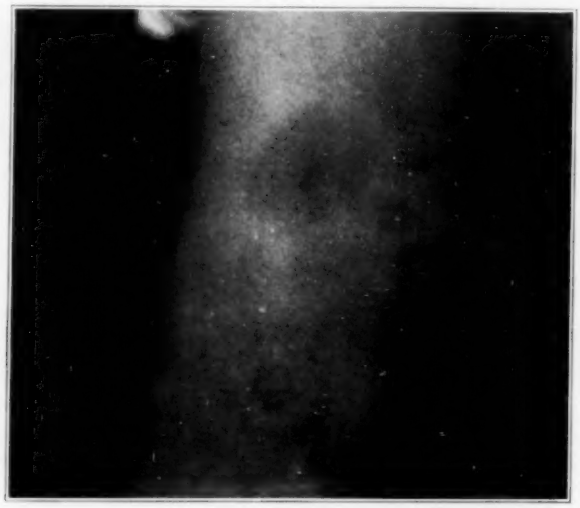
28. Cooke, R. A., in Tice, Frederick: Practice of Medicine, Hagerstown, Md., W. F. Prior Company, 1924, vol. 5, p. 503.

RESULTS

Fifty patients, thirty-three with eczema, fourteen with urticaria, one with erythema multiforme, one with angioneurotic edema and one with generalized dermatitis, ranging in age from 2½ to 66 years, were tested by the intradermal and scratch methods with thirty-two corresponding food proteins.

The total number of tests done with the intradermal method were 356, and a corresponding number of tests were done with the scratch method.

Among the fifty patients tested, eight reacted negatively with the intradermal method, an incidence of 16 per cent. With the scratch method, twenty-seven reacted negatively, an incidence of 58 per cent.



Intradermal delayed reaction to wheat which on the previous day had been negative. The lower mark is the site of a negative scratch test.

No patients were encountered who gave positive reactions with the scratch method and negative reactions with the intradermal.

Of 356 intradermal tests performed, 155 were positive, an incidence 43.54 per cent. The corresponding reactions with the scratch method were definitely positive in 55 of 356 tests, an incidence of 15.45 per cent.

In the entire series, with the intradermal method, forty-two patients reacted positively to one or more food substances, an incidence of 84 per cent, while with the scratch method, twenty-one reacted positively, an incidence of 40.2 per cent.

From these figures, it will be noted that the intradermal test resulted positively in forty-two of the fifty patients with clinical diagnoses of

allergy, and that the scratch test, with the corresponding dry preparations, resulted positively in twenty-one patients; in other words, the results show that the scratch method as compared with the intradermal method detected food sensitization in only one-half the cases, or 50 per cent less.

In the group of forty-two patients who gave positive reactions, single sensitization occurred in three with the intradermal method, an incidence of 7.14 per cent. None occurred with the scratch method.

Within twenty-four hours, patients were examined for delayed reactions. Positive delayed reactions were observed in those in whom the immediate reactions had already been clearly positive, but of course the evidence here was merely confirmatory. In fifteen of twenty-three patients who gave such reactions with the intradermal method, the diagnosis was based on the delayed reaction alone, the immediate reading

Summary of Corresponding Reactions to Food Substances with the Scratch and Intradermal Methods

Skin Reactions	Scratch Method	Intradermal Method
+	32	82
++	4	48
+++	3	12
Plus reactions	39	142
Plus-minus	16	13
Positive total	55	155
Negative	301	201
Total	356	356

Percentages: Scratch total positives = 15.45
Intradermal total positives = 43.54

being no stronger than doubtful. This is an incidence of 4.2 per cent. With the scratch method, five positive delayed reactions were noted, and in three of the five the diagnosis was based on the delayed reaction alone, an incidence of 0.84 per cent.

Plus-minus reactions were encountered with both methods. Only the more striking ones were recorded with the intradermal, whereas with the scratch method, all reactions stronger than the control were considered positive. This interpretation is in accordance with the standards for this method. Incidentally, sixteen plus-minus reactions were recorded with the scratch method and thirteen with the intradermal.

Immediate constitutional reaction occurred in one case. This patient, 16 years of age, had had eczema since infancy, with occasional attacks of asthma. She gave the history of being hypersensitive to eggs and wheat. She was tested for wheat by both methods, and a mild attack of asthma immediately developed. The local scratch reaction was twice as large (2.5 by 3.0 cm.) as the intradermal reaction. Since both tests were performed simultaneously and each was positive, one or the other

or both may have been responsible for the constitutional reaction. But, in view of previous experience, it is reasonable to assume that the cause of the reaction was intradermal in origin; furthermore, the onset of the constitutional symptoms (dyspnea, cough, etc.) immediately followed the intradermal test.

No infection occurred with either method.

INTERPRETATION OF THE REACTION

Many pitfalls are encountered in the proper interpretation of the reactions to skin tests. The specific local allergic reaction, a wheal surrounded by a zone of erythema, occurs only when the cells of the patient are sensitized. This, in the presence of a negative control test, is interpreted as a positive allergic reaction. Confusion occurs when the reactivity of the skin is excessive. This is especially seen in persons with dermatographia, in whom the slightest trauma to the skin causes a marked angioneurotic local swelling. The reading of the results of the intradermal method in these patients is particularly difficult, for the control as well may give characteristic wheals with irregular pseudopods and wide zones of erythema. When such reactions occur, it is best to delay the reading for an hour or more, because during that time the element of trauma in the reaction usually fades away. In these patients, the cutaneous method may prove less confusing. Trauma also causes nonspecific reactions in some persons who are more sensitive than others. This is especially true of persons subject to various allergies. The application of some harmless material, such as tenth-normal potassium hydroxide solution on an abrasion or the injection of a physiologic solution of sodium chloride may elicit a characteristic wheal. This, in the interpretation of the test, introduces a source of error and must be checked in every case by a scarification or intradermal control test.

The oral administration of the iodides and bromides may also influence intradermal skin reactions to the extent of increasing their degree and severity in the skins of persons who are not allergic. Sherrick,[29] in 1915, working with luetin, found that the administration of potassium iodide either simultaneously or shortly before or after the intradermal injection of luetin resulted in the production of a positive cutaneous reaction in healthy nonsyphilitic persons. In 1916, this observation was subsequently confirmed by Lyons[30] and Kolmer and his co-workers.[31] In order to avoid erroneous results, it is important to keep in mind the

29. Sherrick, J. W.: The Effect of Potassium Iodid on the Luetin Reaction, J. A. M. A. **65**:404 (July 31) 1915.

30. Lyons, R.: The Influence of Potassium Iodid on the Luetin Test, South. M. J. **9**:487, 1916.

31. Kolmer, J. A.; Matsunami, T., and Broadwell, S.: The Effect of Potassium Iodid on the Luetin Reaction, J. A. M. A. **67**:718 (Sept. 2) 1916.

influence of the iodides and bromides on cutaneous reactions, especially when the intradermal method is employed.

In recording the degree of reaction (1 plus, 2 plus, etc.), it is well to remember that the location of the test influences the reaction. Schloss,[14] Brown,[15] Alexander [32] and Larson and his co-workers [17] stated the belief that the size of the reaction varies, depending on the location of the test. These observers find that the skin near or at the elbow fold anteriorly gives larger reactions than the skin nearer the wrist, and Stier [33] expressed the opinion that the skin between the scapulae and the crest of the ilium is more uniformly sensitive. If the forearm is selected for the site of the inoculation, the control test should be placed nearest the bend of the elbow, since the skin is more sensitive at this place.

In my series, the plus-minus reactions were considered as indicative of sensitization in the presence of a negative control test. Rackemann [34] and Cooke [35] dismissed these immediate small reactions as of no clinical significance. Stier [33] expressed the belief that from the standpoint of response to food tests each allergic patient presents an individual problem. On the other hand, Peshkin [36] claimed that the size of the reaction depends on the concentration of the offending substance in the test material used. One or both of these factors may be responsible for the less striking plus-minus reactions.

Delayed Reactions.—The more recent investigators attach great diagnostic significance to the delayed reactions as indicative of food sensitization. Vaughan,[37] in 1927, and Rowe,[38] in 1931, put much stress on the delayed or erythematous reactions. Schamberg [39] entertained the same opinion. In my series, such reactions occurred with both methods and were recorded as positive. With the intradermal method, the delayed reactions occurred five times more frequently than with the scratch method, a ratio of 5:1.

Constitutional Reactions.—Food allergens may cause immediate constitutional reactions by whatever pathway they are introduced sys-

32. Alexander, H. L.: Localized Allergy, M. Clin. North America **11**:399 (Sept.) 1927.

33. Stier, Robert F. E.: Food Sensitization as Determined by Skin Testing: A Preliminary Report, Texas State J. Med. **26**:294, 1930.

34. Rackemann, F. M.: Skin Tests with Foreign Proteins in Various Conditions, Am. J. M. Sc. **87**:163 (Jan.) 1922.

35. Cooke, R. A.: Cutaneous Reactions in Human Hypersensitiveness, Proc. New York Path. Soc. **21**:8 (Jan.-May) 1921.

36. Peshkin, M. M.: Asthma in Children: I. Etiology, Am. J. Dis. Child. **31**:763 (June) 1926.

37. Vaughan, W. T.: Allergic Eczema, J. Lab. & Clin. Med. **13**:24 (Oct.) 1927.

38. Rowe, A. H.: Food Allergy, Philadelphia, Lea & Febiger, 1931, p. 38.

39. Schamberg, J. F.: Personal communication.

temically, that is, after the scratch test, after injection or on ingestion. Up to the present time, there have been no data with which to compare the relative frequency of general reactions occurring with the intradermal technic as compared to the scratch method of cutaneous diagnosis. It is safe to say that such reactions are expected and encountered more often with the intradermal test, but they also occur with the cutaneous method, as for example the constitutional reaction reported by Smith [6] to buckwheat and by Cooke [3] to timothy pollen. Both used the scratch test. In my series, one immediate general reaction was encountered. As has been stated, both tests were done simultaneously, but in spite of this fact, the general reaction was caused by the intradermal test, since the constitutional symptoms became apparent immediately after the performance of this test. Immediate constitutional reactions do occur more often with the intradermal test, according to the greater number of cases reported in the literature. Several explanations have been offered as to why general reactions are rare with the cutaneous test. Cooke [3] stated that general reactions are infrequent with the scratch test because the dry extract is less potent than the fluid preparations generally employed in the intradermal test, while Peshkin [36] "attributes the rarity of occurrence of general reaction, properly performed, to the edema accompanying a positive reaction which seals the cut and prevents further absorption of the protein. By virtue of its being a scratch test, there is the slowest possible absorption of the protein, and the reaction thereby becomes purely local in its effect."

COMPARISON OF THE TWO METHODS

Some physicians prefer the scratch method because of the relative ease of performing the test. With children either method is difficult. This is especially true of the intradermal technic in which cooperation is essential. However, with adults, less time is employed in giving the intradermal test than is required for the scratch test. Also, less time is required to make the readings as compared with the scratch test.

Objection has been made by some that the intradermal test is more painful. In my series, this is not strictly so; when a fine hypodermic needle is employed the pain is reduced to a minimum. However, discomfort was noted with both methods. Furthermore, the damage with the intradermal test is limited merely to the prick of a fine needle, and the mark as a rule disappears in from one to seven days, whereas with the scratch test an abraded area is produced by scraping and further damage is done by rubbing the test material into a previously traumatized skin. The resulting mark produced by the scratch test is more pronounced and persists for weeks.

The contrasting results of the two methods up to the present time show that the intradermal test is far superior in detecting food sensitiza-

tion in suspected allergic persons. The reactions are more immediate, reliable and clearcut. It is true that nonspecific reactions are apt to occur with the injection method, but when the tests and the control test are carefully performed and interpreted, the intradermal test is still the method of choice.

Constitutional reactions have been reported to occur with both methods. All factors being equal, it should be expected that such reactions would be more frequent with the intradermal method, since it is an injection test, and as such the absorption of the allergen is more direct and immediate.

Schloss [14] mentioned the possibility of infection resulting from the intradermal test. This danger is easily eliminated by the employment of proper aseptic precautions in the preparation of the fluid allergens and in their use.

COMMENT

Since the use of the skin test is based on the assumption that in allergy the cells of the skin share in the sensitization, a local reaction of allergic shock should be produced in a previously sensitized person when an allergen in a suitable form is applied to an abrasion of the skin or injected intradermally. Customarily a local reaction develops in an allergic person after contact with a specific allergen to which he is sensitive. By means of the skin reaction investigators have found this to occur in more than 50 per cent of cases of food allergy. Of the two methods commonly employed, the intradermal has proved more sensitive and more reliable, and consequently more positive allergic reactions have occurred with it than with the scratch method. Is there a distinct advantage of one method over the other, or is it a question of activity and potency of the corresponding liquid and dry allergens employed that causes one method to be more sensitive than the other?

As for the method, there is no doubt that with the intradermal route a more clearcut immediate reaction is to be expected, as well as an occasional constitutional reaction, owing to more rapid absorption taking place as a result of the direct method of introducing the allergen. With the scratch method, the corresponding dry allergen being employed, one would expect an identical allergic reaction, though it may not be as immediate or clearcut, owing to slower absorption by the lymphatics. However, the reactions of the two methods, read within a reasonable length of time (from one-half to one hour) should be almost identical.

In regard to the question of activity and potency of the liquid and dry allergens, it appears that there must be a difference between the two, judging from the results reported by numerous investigators on the subject of food allergy. This existing difference may be that the liquid allergens are more potent than the dry extracts. Owing to numerous negative reactions in persons known to have food sensitization, it is safe

to state that the potency and activity of the dry preparations are questionable and unreliable. Indeed, there is no way in which to tell when they have lost their potency. In respect to the liquid allergens it is possible to know whether or not a solution is reliable for use. With solutions, contaminations that destroy the potency can readily be seen. The formation of a precipitate reveals that the potency is decreasing or is entirely destroyed.

In the present communication the contrasting results of the two methods are evident. In reference to the intradermal method, objection may be made that the percentage of positive reactions is rather high. The explanation for this is that only patients clinically found to be allergic were tested, and that all the food proteins were not employed as a routine, but only those which came under suspicion in each patient.

In six patients (12 per cent) the liquid allergens were also employed in performing the scratch test. The results have not been included in the report, since the investigation in question concerns only the comparative value of the liquid intradermal test and the dry scratch test. However, it may be stated that incidentally the results were identical with those of the intradermal tests; that is, when one was positive, the other also was positive, etc.; the only difference noted between the two methods was the degree of reactivity. The positive reactions obtained with liquid scratch tests were not as clearcut as those with the intradermal tests. Also, it was observed that in many instances the dry allergens gave plus-minus or negative reactions while the liquid allergens gave a distinct positive reaction with both methods. This observation would lead one to believe that the fault is not so much with the method as with the form and concentration of the allergen employed. In hypersensitive patients, especially those who have the so-called eczema-asthma-hay fever complex, it would be advisable to employ the scratch method with the liquid allergen, thereby minimizing the possibility of a constitutional reaction, which most frequently occurs in this class of patients.

SUMMARY

In a group of fifty patients clinically suspected to be sensitive to one or more food proteins, the intradermal test resulted positively in forty-two, or 84 per cent. The cutaneous test, with the corresponding dry preparations resulted positively in twenty-one patients, or 40.2 per cent.

The total number of positive reactions obtained with the intradermal method were 155 of 356 tests, or 43.54 per cent. The corresponding reactions with the cutaneous method were definitely positive in 55 of 356 tests, or 15.45 per cent.

Delayed reactions occurred with both methods. Diagnosis was based on the delayed reaction alone in fifteen patients with the intradermal method, and in three patients with the cutaneous test.

Single sensitization occurred in three patients, or 7.14 per cent, with the intradermal method. None occurred with the scratch method.

Immediate constitutional reaction occurred in one patient with the intradermal method, an incidence of 2 per cent. None occurred with the scratch method.

In the process of testing, both methods caused discomfort. The resulting marks produced by the scratch test were more pronounced and persistent as compared to those resulting from the intradermal test.

Less time is required for applying the intradermal test and for obtaining the results than is needed for the scratch test.

CONCLUSIONS

The intradermal method of testing, if carefully performed and interpreted, is superior to the scratch method. It is more sensitive and more reliable. Questionable positive reactions must be measured parallel with the results of the control test.

NOCARDIOSIS CUTIS GANGRENOSA

W. H. GUY, M.D.
AND
T. R. HELMBOLD, M.D.
PITTSBURGH

Since Nocard in 1888 described a sporothrix as the cause of *"farcies du boeuf,"* a variety of clinical conditions affecting man and animals have been ascribed to infection by Nocardia. This group of organisms has been most frequently reported in subcutaneous abscesses, particularly those about the mouth or neck. Many of these cases were, however, apparently actinomycosis, the differential diagnosis being established in many cases by minor morphologic and cultural departures from Actinomyces bovis. Nocardia has frequently been reported as an etiologic factor in cases of pulmonary disease simulating tuberculosis. Several cases of cerebral abscess have been reported. Nocardial infections of the tonsils, intestinal tract, appendix and bronchi have been reported. Infections of the skin apparently are rare. Most numerous, perhaps, are cases of pseudo-actinomycosis and of mycetoma from which some member of the genus Nocardia has been recovered. In 1896, Rosenbach [1] isolated Streptothrix from a case of dermatitis which he called erysipeloid. In 1902, Du Bois St. Séverin [2] recovered Nocardia in a case of ulcerative conjunctivitis. In 1904, Lasserre [3] found Nocardia in an ulcerative lesion of the pharynx and the upper lip. In 1909, Pinoy and Ravaut [4] described a peculiar nodular condition of the subcutaneous tissues and muscles due to Streptothrix. A similar organism was isolated, in 1912, by Langeron and Chevalier [5] from a patient presenting peculiar whitish, dry, squamous patches on the skin. In 1913, Potron and Thiry [6] reported a case of nocardiosis involving the skin of the neck with small vesicles, crusts and pustules resembling

---

From the Department of Dermatology School of Medicine, the University of Pittsburgh.

Read at the Fifty-Fifth Annual Meeting of the American Dermatologic Association, Havana, Cuba, May 5, 1932.

1. Quoted by Castellani and Chalmers: Manual of Tropical Medicine, ed. 3, New York, William Wood & Company, 1920, p. 1058.
2. Du Bois St. Séverin,[1] p. 1060.
3. Lasserre,[1] p. 1061.
4. Pinoy and Ravaut,[1] p. 1066.
5. Langeron and Chevalier,[1] p. 1059.
6. Potron and Thiry, G.: Pyodermatomycose provoqué par un "Nocardia," Rev. méd. de l'est **45**:159, 1913.

impetigo. In 1916, Macfie [7] discussed trichonocardiosis, a disease affecting the hair shafts of the axillae and groin. In 1918, de Korte [8] reported a case involving the external ear in which a dusky red, brawny swelling extended about 2 inches (5 cm.) around the insertion of the ear. In 1920, one of us (Dr. Guy) [9] reported a case simulating sporotrichosis in which Nocardia was found by culture and section. In 1925, Gougerot [10] reported a group of cases showing elephantiasic ulceration at or near the mucous outlets; some were due to the tubercle bacillus and others were credited to Nocardia. It is to be noted that these cases are due to related but not identical organisms, members of the same group. Final classification has been difficult on account of the large number of subvarieties of Nocardia and the confusing nomenclature. The following case is reported because Nocardia was demonstrated by culture of the blood and of the tissues and by section.

REPORT OF CASE

History.—A housewife, aged 36, prior to the onset of the cutaneous condition, had lost 60 pounds (27.2 Kg.) over a period of three years, owing apparently to financial and other worries. The family and past histories were essentially irrelevant. When the patient was first seen by us, the condition of the skin was of forty weeks' duration. The first lesion noted was a "blind boil" near the umbilicus, which did not "point," but which spread under the skin laterally almost to the crest of the ileum, the center becoming gangrenous and sloughing to the musculature. Chills and fever and a bloody dysentery accompanied the appearance of the cutaneous lesions. The ulceration healed slowly by granulation, leaving a depressed scar. The lesion was extremely painful until the slough separated, following which the distress was relatively slight. Soon after the first lesion healed, the left leg became involved in the same manner, the process beginning on the calf and extending from the ankle to a point about 10 cm. below the knee. The same general symptoms accompanied the appearance of this lesion, and healing proceeded slowly after the separation of the slough, some ulceration still being present when we first examined the patient. While the lesion of the leg was sloughing, a similar lesion appeared on the left thigh, which extended to a diameter of approximately 12 cm. Again the same general symptoms accompanied the process. When healing was partially completed, the right breast became involved; at this time the patient came under our care and was hospitalized. Prior to this she had had a total of seventeen gangrenous sloughing lesions, all of which, except those noted, were small and not marked by any particular general manifestations.

Examination.—The lesion of the breast appeared as an erythematous, painful, subcutaneous, somewhat elevated nodule. Within twenty-four hours, an edematous,

---

7. Macfie, J. S.: A Fourth Variety of Trichonocardiosis, Ann. Trop. Med. **10**:283, 1916.

8. de Korte, W. E.: Nocardia Cylindracia: A South African Otomycosis, Ann. Trop. Med. **11**:265, 1917.

9. Guy, W. H.: Nocardiosis Cutis Resembling Sporotrichosis, Arch. Dermat. & Syph. **2**:137 (Aug.) 1920.

10. Gougerot, H.: Tuberculose et nocardoses elephantiasiques ulcereuses, Presse méd. **33**:1126 (Aug.) 1925.

slightly elevated cellulitis surrounded the lesion, the border advancing at the rate of about 2 cm. every twenty-four hours. After the total diameter reached approximately 8 cm., the central area became gangrenous with an extension of the gangrene each day in keeping with the advancing sharply marginated cellulitis. With the separation of the slough, an ulcer with ragged undermined edges, extending into and in places through the subcutaneous fat, was formed. Tenacious yellowish-white pus bathed the base of the ulcer, and could be expressed from the undermined edges. Chills, a septic temperature, headache, malaise and, in short, the symptoms common to all acute infectious diseases accompanied the development of the cutaneous manifestations.

Treatment.—Healing was extremely slow by granulation until a transfusion of 250 cc. of blood from a suitable donor was given and compound solution of iodine, U. S. P., was administered intravenously in ascending dosage every second or third day, as suggested by Bedford Shelmire,[11] when healing was rapid and complete. No new lesions appeared. Iodides had previously been given by mouth without effect. Later a colloidal iodine preparation was given intravenously daily, because

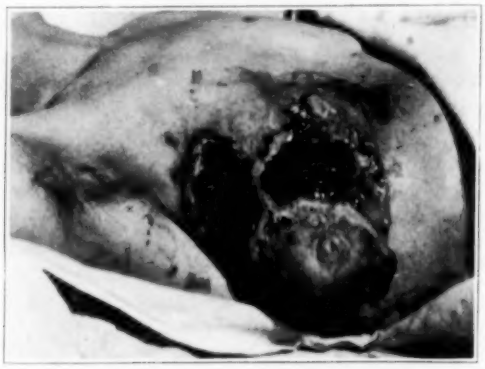


Fig. 1.—Lesion of the right breast.

compound tincture of iodine caused sclerosis of the veins, and spasm of vessels during injections made its administration difficult. After three weeks, the patient was out of bed and had gained approximately 20 pounds (9 Kg.), and all the lesions of the skin were healed, save a granulating area about 2 cm. in diameter on the right breast. Prior to the administration of this therapy, roentgen examination had revealed a well marked peribronchial infiltration, and on proctoscopic examination numerous superficial ulcerations which bled on manipulation were found in the upper part of the rectum and sigmoid.

Laboratory Data.—During the febrile period, the leukocyte count was never higher than 12,000 per cubic millimeter, the differential count showing little departure from normal. Moderate secondary anemia was demonstrated. Chemical examination of the blood early in the course revealed an increase in the nonprotein nitrogen and urea nitrogen, which reached the normal level after the patient had been in bed for ten days. The Wassermann reaction was repeatedly negative. A

11. Shelmire, B.: Intravenous Iodine Therapy, Texas State J. Med. **22**:644 (Feb.) 1927.

therapeutic test gave negative results. A general survey of the case by various members of the staff of the South Side Hospital revealed no additional findings of moment.

Bacteriologic Data.—A culture of the blood was made immediately following a chill while the temperature was 102.8 F. This culture remained sterile until the eleventh day, when a growth of tangled gram-positive slender threads was found both in the original broth and in the daily transfer tubes, the controls remaining sterile. This organism occurred as tangled threads with true branching, and showed the formation of conidia after three days' growth on artificial culture mediums. As the cultures became older, thread forms rapidly disappeared, being replaced by spores occurring as single forms and in short chains. A few short rods with slight terminal swellings were noted. The thread forms were nonseptate, and all forms were nonmotile. Young cultures were definitely gram-positive, but on aging gradually became gram-negative. As the staining reaction changed, an irregular deposit of the gram-positive staining material produced a stippled appearance. The spores also lost their gram-positive characteristics on aging. All forms showed a nonacid-fast reaction. The organism grew on all artificial mediums both at 21 C. (68.8 F.) and 37.5 C. (99.5 F.), the growth being much more rapid at the latter temperature. The organism was an aerobe and a facultative anaerobe. It grew slowly and with difficulty as an aerobe after having been cultured as an anaerobe. The organism liquefied gelatin and peptonized milk slowly, with the formation of a slight amount of acid. Blood pigment was slowly destroyed, with a gradual but wide distribution of the hemolytic substance. In plain broth growth was noted first at the bottom of the tube as delicate, fussy, translucent masses, with the formation later of disk-shaped, firmer, light grayish masses, which tended to float at different levels, gradually coming to the surface. Here the growth became confluent, with the production of a folded, piled-up, rather tough grayish membrane, the surface of which gradually assumed a white, powdery appearance. On solid mediums growth began as a small, glistening, but dry, firm, gray colony which was very adherent to the surface. In mediums containing considerable fluid, such as Loeffler's blood serum, these characteristics tended to be maintained. On solid mediums with a dry surface, this appearance soon changed to that of a folded, thick, piled-up, white colony, changing to a pale brown one with a powdery surface. In all of the cultures a strong musty odor was noted. Hanging drop cultures showed radiating masses of refractile tangled threads, with the formation of spores on aging. Cultures of blood taken when the patient was afebrile remained sterile.

Tissue measuring 2.5 cm. in width was removed from the gangrenous slough of the breast and from the center of the spreading cellulitis. This area was gangrenous the following day. The tissue was divided for culture and histologic study. Aerobic and anaerobic cultures were prepared. The aerobic cultures were discarded because the mediums were overrun by organisms belonging to the ordinary flora of the skin. The anaerobic preparations remained sterile until the thirty-seventh day, when a pure growth of the same organism as that isolated from the blood was recovered. The medium used was a dextrose serum agar containing cubes of human tissue.

In systemic bacteriology the organism falls into the class of Schizomycetes, order Actinomycetales, family Actinomycetaceae, genus Actinomyces. Further classification of the organism at this time is impossible, unless one accepts the classification of Trevisan (1889), who suggested the name Actinomyces for the nonspore-bearing and Nocardia for the spore-bearing forms of Actinomycetaceae. A detailed study of this organism will be presented in a future communication.

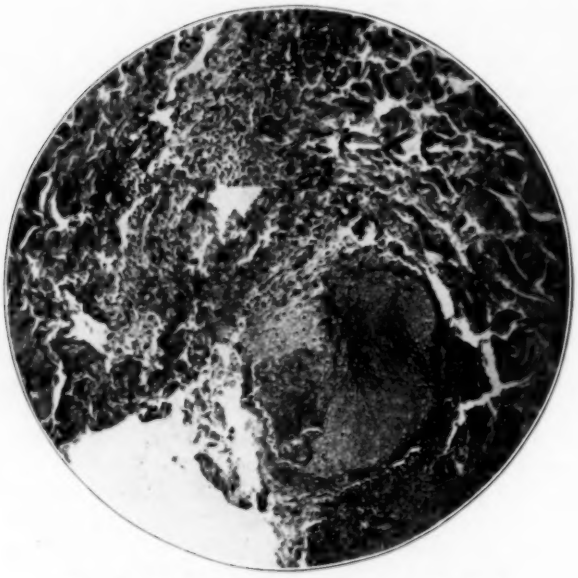


Fig. 2.—Thrombosed vessel deep in the cutis.

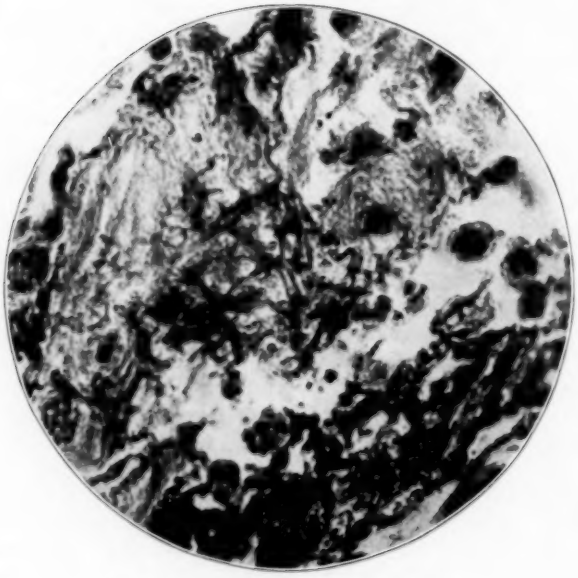


Fig. 3.—Nocardia in the deep cutis.

The name we have applied to the clinical condition reported herewith is perhaps justified by the preceding facts.

Cultures and smears of the exudate from the ulcers revealed staphylococci, streptococci and gram-positive bacilli.

Histologic Data.—The changes in the epidermis were apparently secondary to an underlying pathologic process. Parenchymatous and interstitial edema were noted in the rete, with the presence of a few polymorphonuclear leukocytes. The corneous layer showed a tendency toward separation by edema. The principal changes were in the dermis. Edema, most marked in the papillary zone with the engorgement of the vessels, was noted. The deeper vessels were thrombosed. There was present a wide zone of perivascular infiltration comprised predominately of polymorphonuclear leukocytes, with a scattering of lymphocytes, monocytes and plasma cells. There was a moderate diffuse infiltration of the same character, most marked in the papillary zone. Minute foci of coagulation necrosis of collagen occurred throughout the section. The elastic tissue was swollen, but not disarranged. Gram-Weigert preparations revealed foci of filaments near the vessels, and, in one instance, in a thrombosed vessel.

COMMENT

It seems probable that nocardial infections of the skin are more frequent than is recognized. Similar clinical conditions have been reported from time to time under the name of pyodermia (ecthyma) gangrenosum. A review of the literature at this time with reference to similar cases seems superfluous. The report by Brunsting, Goeckerman and O'Leary [12] records similar cases and gives an excellent review of the literature.

The lowering of resistance seems to stand out as a predisposing factor in most cases. Our patient lost 60 pounds prior to the onset of the lesions on the skin. Certainly the association of gangrenous sloughing ulcers, bloody diarrhea, with ulceration of the rectum and sigmoid, and general manifestations is a distinctive clinical picture. We interpret the condition as an embolic process with dissemination of the infection by way of the blood stream, perhaps, in this case, from the gastrointestinal tract. This fact is suggested by the histologic observations and by the fact that we recovered the organism from the blood stream following a chill and during a septic type of febrile movement.

DISCUSSION

Dr. Fred Wise, New York: We seem to have again an example of an important cutaneous manifestation which has been, one might say, "discovered" by Dr. Guy and the men working in his laboratory. Even if only one case has been demonstrated as being definitely due to Nocardia, it is still an important advance in our knowledge. When I think of the many cases of chronic ulcers and deep-seated serpiginous lesions of the type described by Dr. Guy, which we see in hospitals that harbor patients for months and years (such as the city hospitals), it

12. Brunsting, L. A.; Goeckerman, O. H., and O'Leary, P.: Pyoderma (Ecthyma) Gangrenosum, Arch. Dermat. & Syph. **22**:655 (Oct.) 1930.

brings to mind the fact that the consultants used to stand around the beds of such patients, discussing them at length and advising all sorts of serologic and other examinations, and still it has been unusual to discover the causative organism. There are many cases of the type described in which it has been impossible, even by the most careful work, to isolate the inciting organism.

It should be emphasized that in some of these cases no complicating element is present. Whether Nocardia plays a rôle or has anything to do with the non-gangrenous types of serpiginous ulcers is an interesting subject for further research.

Dr. Fred D. Weidman, Philadelphia: This is the second case of nocardiosis cutis which Dr. Guy has reported; the first case was of the furuncular type, and now nocardiosis cutis gangrenosum is on the dermatologic map. I had the privilege of seeing this patient in Dr. Guy's hospital ward and of studying the cultures in my laboratory. So thoroughly has this case been studied that only one criticism might be offered, namely, that auto-inoculation was not practiced. However, in this case the presence of the organism in the blood and the lesion makes such a procedure unnecessary. Incidentally, the increasing number of cases reported at this meeting in which auto-inoculation has been practiced is most gratifying. This procedure represents an advance in our methods, and certainly should be practiced in all cases in which an additional lesion can be of little moment to the patient.

The classification of the organism has been closely considered. Every promise is given that it can be assigned a definite taxonomic place in bacteriology because for Nocardia it is distinctive in culture.

Dr. Wise raised the question of making a culture in these cases. Certainly, culture of the blood is warranted in any dermatologic condition having febrile aspects. In the epidemic of Haverhill disease, with its erythema multiforme, the causative organism was isolated from the blood and synovial fluid, and it was the similar success of Drs. Guy and Helmbold that paved the way to rational and successful therapy. It must be a great satisfaction to these authors to witness such good results in the treatment of their patient; when I saw her she was almost moribund. If the iodide therapy was responsible for her recovery, it must in turn be referred to the accurate diagnosis without which there could not have been a rational therapy.

Dr. Michael H. Ebert, Chicago: I think that in this type of disorder, the presence of the anemia should be emphasized as an important factor in its production. I believe that there was severe anemia in this case and in the majority of cases reported by Brunsting from the Mayo Clinic. I had an opportunity to study a case in the Presbyterian Hospital, in Dr. Ormsby's service, in which the condition was almost as severe as that in the cases shown at this meeting. I think that my associates and I were influenced by Dr. Mook's work, and we started a long hunt for an ameba but could not find it. Dr. Ormsby left the city, and before he left I asked him how long he thought the patient would survive; he said he thought about a week. Transfusions of blood were given, with no other treatment of any moment, and the man soon went home in good condition. The last communication we had from him stated that he was an applicant for life insurance and wanted to explain his stay in the Presbyterian Hospital. He had had severe anemia and was at the point of death at one time; I think that anemia plays an important rôle in all such cases. In another case seen at the Cook County Hospital, in which there was a question as to whether the condition was a pyodermic or a streptococcic infection, with marked anemia, the patient was similarly treated. As soon as the anemia began to disappear, the condition of the skin improved and complete recovery ensued.

DR. T. R. HELMBOLD, Pittsburgh (by invitation): This report has been conclusive, and I can add only a few remarks concerning the cultures.

The blood culture remained sterile until the eleventh day and the tissue cultures until the thirty-seventh day. We anticipated considerable trouble with contaminators when we cultured the tissue, and in this we were not disappointed, since in the aerobic preparations many ordinary bacterial forms grew rapidly. This happened in spite of the fact that we employed a high degree of asepsis in collecting the material and a bath of a 70 per cent solution of alcohol followed by one of sterile water before placing the tissue into the mediums. In addition to the aerobic cultures, the tissue was placed in a number of mediums in which a high degree of anaerobiosis was obtained; these cultures remained sterile until the thirty-seventh day, when the organism grew in the mediums developed by Dr. Jacob and myself for our work in lichen planus. The other anaerobic preparations, however, all became positive within the next few days. I have nothing further to add, except that we have been unable to find a classification which will fit this organism.

DR. WILLIAM H. MOOK, St. Louis: I also wish to congratulate Dr. Guy on the thoroughness and completeness of his work, and to agree with Dr. Wise's remarks on the question of ulcers. Formerly we could not classify these cases satisfactorily. The work that Dr. Wise has done greatly resembles that done by Engman on amebas of the skin, and it accounts for many cases in which no bacteriologic evidence could be found.

DR. WILLIAM H. GUY, Pittsburgh: Dr. Wise raised the question of the possible relationship of infection by Nocardia and gangrene. I think that the gangrene can be explained by the deep thromboses cutting off the circulation, and that Nocardia was the offending organism. I may refer to the case I reported several years ago in which Nocardia was found in the tissue and the blood stream in a case resembling that caused by Sporothrix. In that case there was no gangrene, so it is plausible that the anatomic conditions are responsible for the gangrene. We have attempted to keep to the bacteriologic classification used by pathologists rather than that used by mycologists, because so often objection is raised regarding the terms.

Dr. Ebert properly mentioned the excellent results of transfusion of blood. In the cases reported in the past, nearly all of the patients have been treated by transfusions of blood, many of them by no other treatment. Apparently a marked lowering of resistance is required before the infection occurs. In our case the patient lost 60 pounds before the condition manifested itself.

Dr. Mook mentioned his cases. We are not saying that this is the only cause, and should like to see cases investigated along this line, cultures of the blood being obtained during the febrile period, during the height of the attack and while the patient is febrile. An article appeared recently regarding hospital gangrene. I think that in this condition the predisposition and the character of the cutaneous lesions are almost the same as in the case reported; however, many of the manifestations that appeared in this particular case are lacking. When one considers that the patient had seventeen small lesions, without general manifestations, and only four of the large ones, it is conceivable that such nocardial lesions might exist.

MYCOSIS FUNGOIDES IN MOTHER AND IN DAUGHTER

OLIN J. CAMERON, M.D.
Instructor in Dermatology and Syphilology, University of Michigan Medical School
ANN ARBOR, MICH.

Major types of lymphoblastoma, that is, leukemia, Hodgkin's disease and lymphosarcoma, as well as mycosis fungoides, have been shown to merge into each other in the same person in numerous cases (Keim,[1] Fraser [2] and Wile [3]).

There are many instances of familial leukemia on record. Striking cases have been cited by J. Chalmers Cameron,[4] Sanger [5] and von Brügger.[6]

Hodgkin's disease has been well reviewed and studied, as regards its familial occurrence, by Arkin.[7] He found cases reported in twins (Peacock and Senator), in a brother and sister (Degen) and in a woman and two brothers (Braun). Arkin himself reported mediastinal Hodgkin's disease in a man, in his son and in his nephew.

REPORT OF CASES

I have been unable to find in the literature reports of two cases of mycosis fungoides in the same family. I believe that the following two cases are the first of such instances to be recorded.

CASE 1.—*History.*—Mrs. L. L., an American housewife, aged 45, came to the clinic on May 11, 1922. She complained of marked itching of the entire body; it had been present intermittently for six years, starting in association with an area of redness on the left thigh. More patches had appeared on various parts of the body and had been occurring on the face for four years. Some lesions had disappeared spontaneously as new ones appeared. No type of treatment had given her any relief from pruritus. There was no family history of tuberculosis, cancer or similar conditions. She had been married for twenty-three years. The husband was living and had "heart trouble." The patient had had fourteen children, only

---

Studies and Contributions of the Department of Dermatology and Syphilology, University of Michigan Medical School, service of Dr. Udo J. Wile.

1. Keim, H. L.: The Lymphoblastomas: Their Relationships, Arch. Dermat. & Syph. **19**:533 (April) 1929.

2. Fraser, J. F.: Mycosis Fungoides: Its Relationship to Leukemia and Lymphosarcoma, Arch. Dermat. Syph. **12**:814 (Dec.) 1925.

3. Wile, U. J.: Ann. Int. Med. **5**:1103 (March) 1932.

4. Cameron, J. Chalmers, in Osler, William: Practice of Medicine, ed. 8, New York, D. Appleton and Company, 1909, p. 732.

5. Sanger, in Osler.[4]

6. von Brügger: München. med. Wchnschr. **74**:683 (April 22) 1927.

7. Arkin, A.: Am. J. M. Sc. **171**:669 (May) 1926.

two of whom were living, the remainder having died shortly after birth from intercurrent infections.

Examination.—Examination revealed a well nourished woman. The skin of the entire body and extremities was diffusely erythematous and scaly. Associated with this were many poorly defined patches of thickening. There were many areas of infiltration, of various sizes and shapes, which tended to be circular, dull red and extensively excoriated. There was less scaling on the face, but involving the forehead and upper half of the nose there was a similar purplish-red area of infiltration. All of the superficial lymph glands were slightly enlarged; the edge of the liver could be felt just beneath the margin of the rib; the spleen was not palpable.

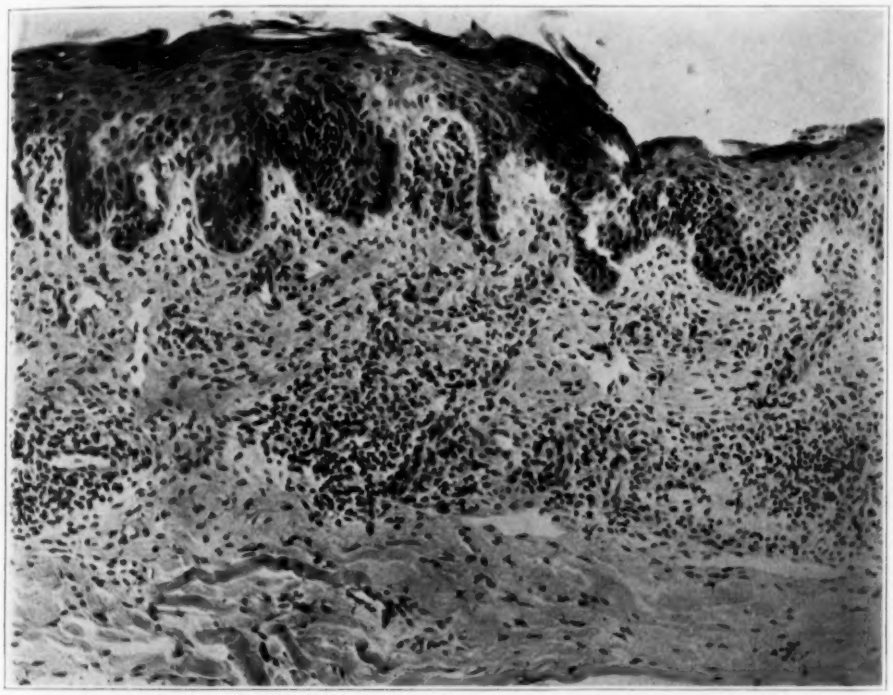


Fig. 1 (case 2).—Microscopic appearance of an early, infiltrated lesion. There is a bandlike papillary and subpapillary infiltrate.

The blood count was normal, the white blood cells numbering 6,350; the only point of interest in the differential count was the presence of 7 per cent of eosinophils.

Course.—The patient was observed and treated over a period of three years, during which time the course of the mycosis fungoides was typical. She received extensive superficial roentgen irradiation and intravenous injections of radium chloride. At first these measures were beneficial, producing involution of many of the infiltrated lesions and relief of pruritus. During the third year the lesions appeared more rapidly, with the characteristic late, fungating, ulcerated tumors. The Wassermann test of the blood was always negative and the urine normal. The patient died at her home in February, 1926. No autopsy was performed.

Histopathologic Examination.—A punch biopsy was taken from one of the infiltrated lesions on the patient's back, on March 21, 1925. The epidermis showed some hyperkeratosis and moderate acanthosis. It was intact. The corium showed a bandlike infiltrate, most marked in the papillary and subpapillary layer, but extending well down into the corium, particularly about the blood vessels and adnexa. The cells were large atypical lymphocytes and large mononuclears, with numerous lymphoblasts. There was some formation of giant cells, and plasma cells were frequently encountered. In a few areas there was active proliferation of the fixed connective tissue cells.

Comment.—This case was previously reported by Keim.[1] The mycosis fungoides took the usual course over a period of nine years. At the time of the patient's death her daughter (case 2) was 22 years old and apparently in subjective good health, except for beginning pruritus.

Case 2.—*History.*—Mrs. M. M., a housewife, aged 28, daughter of the patient in case 1, presented herself at the clinic on May 21, 1931, complaining of marked generalized itching of the skin. The patient said that the pruritus had been present from time to time for seven years. A year before entry an oval patch of dermatitis had developed on the left side of the neck; this had gradually increased to the size of a half-dollar and was decidedly pruritic. During the past few weeks her skin had become universally reddened and scaly, and the pruritus had increased so that she was thoroughly miserable. No history of any arsenical medication or of ingestion of other drugs that might produce such an eruption could be obtained. No irritants had been applied to the skin. There had been no loss of weight. She had had the usual diseases of childhood, and said that at the age of 6 she had been confined to bed for several weeks with rheumatic fever. She had had a "light attack" of pleurisy four years before, but there had been no chronic pulmonary or cardiac symptoms.

Examination.—On examination, the patient proved to be a well developed and well nourished woman of 28, normal except for the heart, skin and the lymphatic system. She was found to have rheumatic heart disease, with mitral stenosis but good function. There was a universal eruption, characterized by a rather deep red discoloration, and marked thickening of the skin, especially over the extremities, the flexor surfaces showing accentuation of the lines of cleavage. There were universal fine, branny scaling and marked hyperkeratosis of the palms and soles, diffuse and not punctate; these regions were deeply fissured. There were no lesions in the mouth. The lymph nodes in the superficial chains were all enlarged, those in the inguinal regions being the size of a walnut. The spleen was just palpable; the liver could not be felt.

Course.—It was felt that the patient probably had an exfoliative erythrodermia suggestive of one of the lymphoblastomas. Because of this she was admitted to the ward for study and care. The urine, hair and scales revealed no arsenic on tests. Studies of the blood on June 1, 1931, showed: hemoglobin, 76 per cent; red blood cells, 4,270,000, and white blood cells, 10,000. A differential blood count showed: polymorphonuclears, 61; large lymphocytes, 7; small lymphocytes, 9; mononuclears, 3; eosinophils, 19; basophils, 1, and hemohistioblasts, 1. The platelets were increased in number, and the red cells showed moderate poikilocytosis and anisocytosis. The findings in the blood were reviewed by a competent hematologist, who expressed this opinion: "The blood is that which one would expect in an exfoliative dermatitis (eosinophilia). The presence of hemohistioblasts suggests disease of the spleen."

The urine was normal. The Kahn test of the blood was negative. A punch biopsy taken on May 27, 1931, from the erythrosquamous skin on the back showed

the following changes: perivascular reticulo-endothelial proliferation and moderate lymphocytic infiltration in both the subpapillary and the papillary layer of the corium. Although the papillary changes were not conclusively typical, they suggested that the condition at this time was lymphoblastoma cutis in the early stages.

Baths, bland ointments and a single small (50 roentgens) general superficial roentgen treatment gave some symptomatic relief, and the patient was discharged after ten days in the hospital. She was seen frequently as an outpatient during the next few months; during this time the eruption changed from that of scaly erythroderma to that characterized by two kinds of lesions: one, typical urticarial wheals, and the other, round or oval infiltrated plaques varying from a purplish

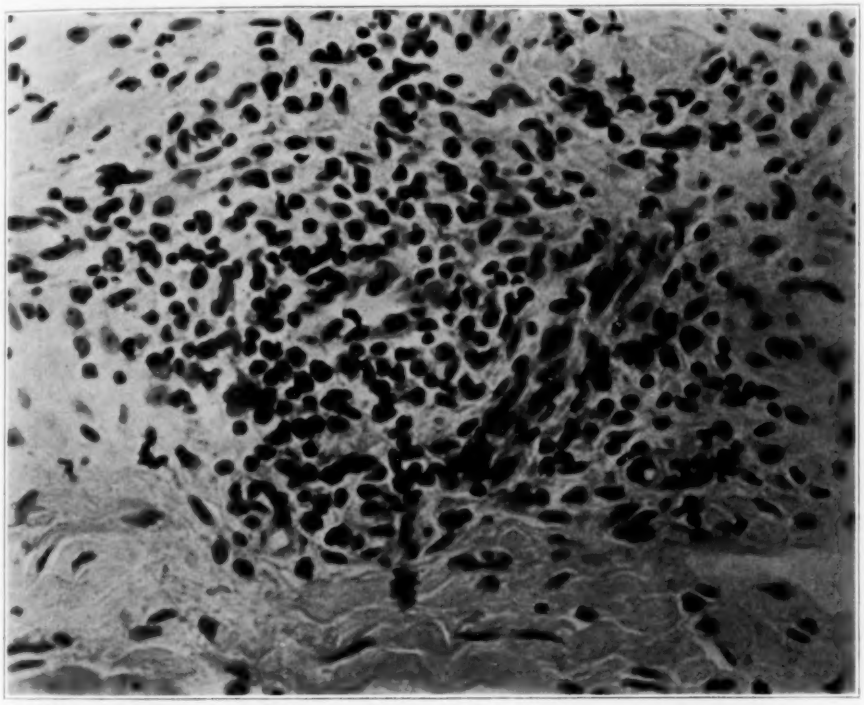


Fig. 2.—High-power photomicrograph of the infiltrate shown in figure 1.

pink to a brownish red. During a period of eight months many pruritic and evanescent wheals developed daily over the surface of the body. Biopsy of one of these showed only edema of the papillary layer. Scratch tests showed positive reactions to many pollens, to a few foods and to a few epidermal substances. Elimination of reacting substances produced no change in the urticaria, but a few weeks after extraction of a devital molar tooth with a septic pocket the urticaria permanently disappeared.

The other type of lesion, namely, the infiltrated plaque, followed the typical course of the infiltrative stage of mycosis fungoides. First, a lesion appeared on the left side of the neck; it was the size of a half-dollar, purplish-pink, sharply circumscribed and infiltrated. It involuted after the attack of exfoliative dermatitis and the stay in the hospital with roentgen treatment. During the last year more

plaques have developed, about a dozen in all; one on the right side of neck involuted spontaneously, and some have been dispersed apparently by a few superficial roentgen treatments (75 roentgens each). The patient has had plaques over the shoulders, neck, back, left hip and thighs. All of the plaques are slightly scaly at times, but their striking characteristics are the sharp demarcation, the purplish or brownish-pink color and the infiltration. The larger plaques are increasing slowly in size, but pruritus is less marked as time goes on.

A punch biopsy taken from the plaque on the upper part of the left thigh showed the following characteristics: slight parakeratosis and acanthosis, but no epidermal edema. There was a diffuse, moderately dense and bandlike infiltrate in the papillary and subpapillary layer of the corium. This showed no predilection to perivascular distribution. The type of cells found were: an abundance of small and large lymphocytes, diffusely scattered; foci of large lymphoblasts intermingled with proliferating fixed connective tissue cells, and a few sparsely scattered eosinophils (figs. 1 and 2). The diagnosis of early mycosis fungoides was concurred in by Dr. C. V. Weller of the department of pathology.

Comment.—The patient in case 2 is the daughter of the woman in case 1; her condition has followed the same course as her mother's. There is a suggestive resemblance in this case to parapsoriasis en plaque, but I feel that there is ample evidence to rule out that diagnosis. The differential diagnostic points that have been worked out by Brocq, J. C. White, J. J. White, Ormsby and Arndt, and reviewed by Wise and Rosen,[8] hold for this case. The application of the observations to case 2 can be summed up briefly as follows:

1. There was a prolonged period of marked pruritus and exfoliative erythroderma prior to the development of the infiltrated plaques; this is not the rule in parapsoriasis, but it is common in mycosis fungoides.

2. The microscopic picture is characteristic of mycosis fungoides and not parapsoriasis.

3. The lesions in case 2 responded to roentgen therapy, as is characteristic in mycosis fungoides; the lesions of parapsoriasis do not respond to roentgen rays.

CONCLUSION

An instance of familial lymphoblastoma, manifesting itself as mycosis fungoides in mother and daughter, with clinical and histologic observations, is recorded.

8. Wise, Fred, and Rosen, Isadore: J. Cutan. Dis. **34**:95 (Feb.) 1916.

SUBCUTANEOUS FAT NECROSIS OF THE NEW-BORN

REPORT OF FIVE CASES

HOWARD FOX, M.D.
NEW YORK

The various types of subcutaneous induration occurring in new-born or young infants have been the source of a good deal of confusion. During the past decade, however, knowledge of the subject has been considerably increased by histologic and chemical examinations.

The type of induration that is the subject of this paper should, I think, be termed subcutaneous fat necrosis of the new-born, though it is still spoken of as sclerema neonatorum by some British and American writers. In many of these cases at the present time the confusion is merely one of nomenclature. Much confusion has also resulted from the reports of cases of scleroderma neonatorum which were manifestly not scleroderma but in all probability cases of subcutaneous fat necrosis. I shall discuss this subject later.

The four principal types of subcutaneous induration to be considered are the following: adiponecrosis subcutanea neonatorum, sclerema adiposum (sclerema neonatorum), sclerema edematosum (edema neonatorum, scleredema) and scleroderma.

Subcutaneous fat necrosis of the new-born, or adiponecrosis subcutanea neonatorum to use the Latin term, has been described under such titles as the following: circumscribed fat sclerosis in nurslings, curable cutaneous induration of the new-born, sclerema adiposum in patches, so-called scleroderma of the new-born, obstetric lipophagic granuloma, etc. In the earlier literature, undoubted cases of this disease have been reported as sclerema neonatorum, scleroderma neonatorum and pseudoscleroderma.

The first undoubted case of subcutaneous fat necrosis was recorded by a Russian author, Cruse,[1] in 1875 under the title of "Scleroderma in a New-Born Infant." In the following four years Cruse reported three more similar cases. In 1920 de Bruin [2] collected reports of twenty-

---

From the New York Nursery and Child's Hospital and the Department of Dermatology and Syphilology, University and Bellevue Hospital Medical College.

Read at the Fifty-Fifth Annual Meeting of the American Dermatological Association, Havana, Cuba, May 3, 1932.

1. Cruse, P.: Ein Fall von Sclerodermie (sogenannt Sclerodermia adultorum) bei einem Säugling, St. Petersb. med. Ztschr. **5**:306, 1875; Jahrb. f. Kinderh. **13**:35, 1879.

2. de Bruin, J.: Sclerodermia neonatorum, Nederl. tijdschr. v. geneesk. **65**: 3174, 1921.

five cases including five of his own, and in 1928 Lemez [3] tabulated eighty-five cases of the disease in question.

The first histologic examination was made by Fabyan,[4] an American, in 1907, his report being entitled "Disseminated Fat Necrosis Occurring in an Infant Without Other Lesions." This early report has apparently escaped the attention of continental European writers, who state that the first histologic examination of the disease was made by Triboulet, Ribadeau-Dumas and Debré [5] in 1912. Gray,[6] however, gave his American colleague the credit that was due him. Ten years after the report of Triboulet and his co-workers, those of Keilmann [7] and of Bernheim-Karrer [8] appeared. The excellent studies of the latter did much to bring the disease to the attention of the medical profession. Numerous reports followed, including those of Carol and van der Zande,[9] Woringer and Weiner,[10] Lemez and others, who are quoted by Ehrmann and Brünauer.[11] The second American case was reported by Farr,[12] and others have recently been recorded by DeVel and Bolin [13] and by Skeer.[14]

SYMPTOMS

The clinical manifestations are strikingly similar in the majority of cases. The disease is a self-limited, localized process affecting various sized areas of the body, often in a fairly symmetrical manner.

---

3. Lemez, L.: Beitrag zur Pathogenese der subcutanen Fettgewebsnekrose Neugeborener (sogenannt Sclerodermia neonatorum) an der Hand einer Kaltereaktion des subcutanen Fettgewebes bei neugeborenen und jungen Säuglingen, Ztschr. f. Kinderh. **46**:323, 1928.

4. Fabyan, M.: Disseminated Subcutaneous Fat Necrosis Occurring in an Infant Without Other Lesions, Bull. Johns Hopkins Hosp. **18**:349, 1907.

5. Triboulet, Ribadeau-Dumas and Debre: Sclérème adipeux en plaques, Bull. Soc. de pédiat. de Paris **14**:199, 1912.

6. Gray, A. M. H.: Sclerema Neonatorum, Arch. Dermat. & Syph. **14**:635 (Dec.) 1926.

7. Keilmann, K.: Circumscripte symmetrische Fettsklerose im Säuglingsalter (Die sogenannte Sklerodermie), Ztschr. f. Kinderh. **33**:298, 1922.

8. Bernheim-Karrer: Ueber subcutane Fettgewebsnekrosen beim Neugeborenen (sogenannt Sclerodermie der Neugeborenen), Schweiz. med. Wchnschr. **52**:12 (Jan. 5) 1922.

9. Carol, W. L. L., and van der Zande, F.: Nederl. tijdschr. v. geneesk. **69**:1317, 1925.

10. Woringer, P., and Weiner, G.: La cystosteatonécrose du tissue sous-cutane chez le nouveau-né, Rev. franç. de pédiat. **4**:57 (Feb.) 1928.

11. Ehrmann, S., and Brünauer, S. R., in Jadassohn, J.: Handbuch der Haut- und Geschleschtskrankheiten, Berlin, Julius Springer, 1931, vol. 8, p. 858.

12. Farr, C. E.: Ischaemic Fat Necrosis, Ann. Surg. **77**:513 (May) 1923.

13. DeVel, L., and Bolin, Z. A.: Traumatic Necrosis of the Subcutaneous Fat of the New-Born Infant, Am. J. Dis. Child. **37**:112 (Jan.) 1929.

14. Skeer, J.: Sclerema Neonatorum, Report of a Cure by X-Ray Therapy, Arch. Dermat. & Syph. **19**:732 (May) 1929.

The patients, who are often born after difficult labor, are usually well nourished and not infrequently of large size. The lesions appear from two to twenty days after birth (according to the statistics of Lemez) as deep-seated, indurated areas in the subcutaneous tissue. They vary in size from that of a split pea or a hen's egg to large areas covering the greater part of the back and buttocks, and appear to be slightly elevated above the surface of the skin. The color is usually bluish red at the outset, suggesting at times a phlegmonous process. This disappears gradually, the skin assuming its normal color even before the lesions have softened and disappeared. The surface of the skin is usually smooth. There is no evidence of pain on pressure.

The most striking feature is the induration of the subcutaneous tissue, which does not pit on firm pressure, and which does not allow the skin to be pinched up in folds. The hardness is often described as resembling that of wood or rubber. The indurated areas have a fairly well defined border and may or may not be movable on the deeper parts. The smaller nodular lesions are usually freely movable, though this is not so apparent in the case of extensive areas. Fluctuation has occasionally been noted, and was present in one of my cases. The favorite sites, according to Lemez, are first the back, then the cheeks, next the arms and thighs and then the buttocks. Almost every part of the body may be affected, except the palms and soles, abdomen, inner aspect of the thighs and axillae. The mucous membranes were involved only in a case of Cruse.

The course of the disease includes a period of evolution and one of involution; both processes may be present simultaneously. Softening and absorption of the indurated areas begin from the fifth to the sixth week and are complete as a rule in three or four months. The duration in twenty cases tabulated by Lemez varied from five weeks to five months. The lesions disappear completely, and only in rare instances do they leave any trace such as slight atrophy (Cruse [15] and Pollitzer [16]).

The general health as a rule remains good, the temperature is not altered, and there is a steady, normal increase in weight. The recorded deaths have nearly always been due to some intercurrent disease.

HISTOLOGIC EXAMINATION

The histologic process is definite and has been remarkably similar in the cases that have been reported. The disease involves the entire thickness of the subcutaneous tissue, whereas the epidermis and corium

15. Cruse, P.: Ein zweiter Fall von Sclerodermie bei einem Neugeborenen, St. Petersb. med. Wchnschr. **1**:20 (July 29) 1876.

16. Pollitzer, R.: Su un caso di sclerodermia in un neonato, Riv. di clin. pediat. **19**:435, 1921.

are either normal or show unimportant changes. The process is essentially a necrosis of the fat cells and an infiltration of epithelioid and giant cells. The septums between the fat lobules are edematous and thickened, and elastic tissue is absent in the areas of infiltration. The protoplasmic meshes between the fat cells are thickened and at times surround empty spaces which have the form of elongated needle-like crystals. In the fat cells, which show one or more nuclei and the protoplasm of which appears to be increased, there are numerous needle-like crystals in the form of rosettes or sheaths, possibly composed of fatty acids. The infiltration, which is especially marked at the periphery of the fat lobules, consists of lymphocytes, fibroblasts and giant cells of the foreign body type and occasional eosinophils. This infiltration penetrates at times into the interior of the fat lobules. Some of the giant cells are filled with crystals radiating from the center. At the border of the process, the fibrous bands are highly vascularized and constitute a cicatricial organization of the granuloma. This is, however, only temporary, as there is later a complete restitution to the normal condition with the formation of new fat.

Of the following cases, one was seen in private practice and the others at the New York Nursery and Child's Hospital, service of Dr. Oscar M. Schloss, through whose kindness I am privileged to report them.

REPORT OF CASES

Case 1.—P. R., a white girl, a private patient, was referred for diagnosis on June 25, 1928, at the age of 6 weeks. She was a first child of Jewish parents, the mother being 29 years old. Labor had been unusually prolonged, and forceps had been used. The baby was born at full term in an asphyxiated condition, weighing 7½ pounds (3,400 Gm.). There was considerable trauma in the process of resuscitation. She had been well nourished and apparently healthy since birth and was breast fed. There had been no gastro-intestinal or other illness. The temperature had always been normal. There was no family history of tuberculosis, and the parents were apparently in good health.

The indurated areas were first noticed at the age of 2½ weeks. A month later extensive areas of induration were found on the lower four fifths of the back, buttocks, postero-external aspect of the thighs and upper half of the calves. There were also circumscribed areas in the pubic region and vulva. The affected areas were smooth and bluish red; the color disappeared on pressure and was slow to return when pressure was discontinued. On palpation, there was a boardlike hardness of the integument, which did not pit on firm pressure, and which could not be pinched up in folds. The smaller areas at least were not incorporated with the underlying musculature. The border was somewhat irregular in outline and was fairly well demarcated. The most marked induration was present on the buttocks, in which region the border was rather ill defined. There was no tenderness on pressure in any of the lesions.

When I first saw the patient she appeared well nourished, weighed 9½ pounds (4,300 Gm.) and had a normal temperature. In the course of the next two and a half months there was a gradual diminution in the hardness and redness of the patches, the lesions on the buttocks, the upper part of the back and the vulva

being the last to disappear. On September 10, three months and ten days after the onset and when the baby was about 4 months old, all traces of the disease had entirely disappeared. She had also gained steadily in weight and weighed 14 pounds (6,400 Gm.). A biopsy was performed on July 16 after partial involution of the patches had taken place. She was presented before the New York Dermatological Society on October 23 after complete disappearance of the disease.

The patient was seen recently when she was about 4 years old, and was a normal, well developed child weighing 42 pounds (19.1 Kg.). Although she was moderately fat, there was apparently some atrophy of the subcutaneous fat of the back. This had been noticed by the mother.

CASE 2.—M. E., a white girl, born at the New York Nursery and Child's Hospital on Oct. 13, 1929, was the first child of a Spanish-American father and a German-American mother. The delivery was normal, and at birth the patient weighed 7 pounds and 4 ounces (3,300 Gm.), was well nourished and apparently healthy. The Wassermann test of the mother's blood and that of the umbilical cord were negative.

On the second day an intracranial hemorrhage was suspected, owing to stiffness of the neck. A spinal puncture was performed, but the fluid was normal except for a few red cells. A blood count showed 13,000 white cells with 64 per cent polymorphonuclear leukocytes. The red cells were within normal limits. The patient was discharged from the hospital at the end of ten days apparently in good health and with a normal gain in weight.

The cutaneous lesions were first noticed twenty-five days after birth, and had not changed appreciably when I saw them five days later. They consisted of indurated, apparently insensitive plaques on the back and on the posterior surface of the arms. They were smooth, bluish red, of firm consistency and had fairly well defined borders. There was no pitting on firm pressure, and the infiltrated masses were movable on the deeper parts. A roentgenogram of the chest failed to show any shadows owing to the lesions in the skin. The eruption consisted of six distinct areas. The largest was in the dorsal region and formed a rectangle covering nearly half of the back. The other areas were rather symmetrically located on the upper two thirds of the back of the arms, three on the left and two on the right arm, and varied in size from that of a split pea to that of small coins.

When seen on November 23, the disease was undergoing involution, the patches breaking up into separate areas and becoming smaller and softer. On December 7 they had almost entirely disappeared, and when seen on December 31, nearly two months after the onset, there was no trace of the disease, and the patient was apparently in perfect health. Biopsy was performed on the large area on the back on November 16 before involution had begun.

CASE 3.—A. M., a white boy, born of Italian-American parents, first visited the New York Nursery and Child's Hospital on Nov. 26, 1928, when 1 month old. He was one of seven children. All except one, who had died of empyema, were living and well. There was no family history of tuberculosis. According to the mother, the patient was a full term baby of large size, and had been delivered by a midwife. Labor was said to have been normal, without forceps. At birth there was no cyanosis. The child had been breast fed since birth and had not suffered from vomiting or diarrhea. Physical examination showed a well nourished, normal baby, with the exception of the changes in the skin.

The mother stated that at birth there was a hard patch 1½ inches (3.8 cm.) in diameter between the shoulder blades. This increased rapidly in size, until at the first visit to the hospital it involved the upper two thirds of the back and the

posterior aspect of the deltoid region. It had always been a dark red and showed on palpation a condition precisely similar to that in cases 1 and 2. During the previous ten days small nodular masses in the cheeks and the right nipple had been noticed by the mother. She also stated that a similar hard area about 3 inches (7.6 cm.) in diameter had been present in the groin, but had now disappeared. The patient was removed from the hospital against advice at the end of five days. No change in the lesions or general health was noted during this time.

The patient returned to the dispensary on December 14, when his weight was 11 pounds and 4 ounces (5,100 Gm.), and the temperature 99 F. He was now bottle fed and gaining satisfactorily in weight. The affected areas of the back and the right nipple had apparently increased somewhat in extent, and another small area of hardness had developed about the left nipple. The lesions on the cheeks had not changed.

Examination on Jan. 31, 1929, when the baby was 3 months old, showed no sign of the previous infiltration, which had disappeared without leaving a trace. The mother stated that the lesions had begun to disappear about one month previously. He now weighed 12 pounds and 6 ounces (5,500 Gm.). Permission for biopsy was refused.

Case 4.—V. C., a girl, born at the Metropolitan Hospital on March 7, 1932, was the first child of a Filipino father and an American Negro mother (mulatto), 23 years old. There was no history of tuberculosis in the family. A Wasssermann test of the mother was negative.

The patient weighed 8 pounds and 6 ounces (3,750 Gm.) at birth. Forceps had been used, and after delivery the baby was given hot baths and an intramuscular injection of the mother's blood. A change in the patient's skin first came to the mother's attention on leaving the hospital at the end of ten days. The child was first seen at the New York Nursery and Child's Hospital on March 19, when extensive changes in the integument were apparent. On April 18, when I first saw the patient, the changes consisted of boardlike indurations with a well defined border covering the entire back from the middle of the scapulae, the buttocks, postero-external aspect of the hips and thighs and the greater part of the calves. There was also a hazelnut-sized nodule at the left angle of the jaw, and there were several larger lesions in both deltoid regions. The color was dull red, most pronounced on the back, and suggested the appearance of a phlegmonous process. There were two almond-sized, fluctuating lesions on the back similar to one which had been removed containing needle-shaped crystals.

The child weighed 9 pounds and 13 ounces (4,420 Gm.) on April 14, and was in good general health. She had never vomited or suffered from diarrhea. While in the hospital for four days her temperature ranged between 98 and 100 F.

On April 21, the lesions were notably softer, and the continuity of the extensive areas seemed to be lessening. At this time a biopsy was performed and a roentgenogram was made. The report on the latter was as follows: "An anteroposterior film of the trunk and thighs taken for detail of the soft tissues shows irregular density in the soft tissue between the skin surface and the plane of deeper muscles over the area between the levels of the iliac crest and the midfemur on both sides, but more so on the left. The middle region of the back is not well shown. This altered density is not roentgenologically diagnostic, but is probably related to the condition of fat necrosis clinically noted."

On April 26, the patient was presented before the New York Dermatological Society.

CASE 5.—Baby K., a white girl, was born at the New York Nursery and Child's Hospital on Jan. 3, 1932, of Polish parents. She was the seventh child, four of the others being alive and well. The mother was 45 years old and weighed 236 pounds (106.4 Kg.). The Wassermann test of the mother's blood and of the placental blood gave negative results. The patient weighed 9 pounds and 9 ounces (4,310 Gm.) at birth, following a breech delivery. At birth the vulva was swollen, and there were bruises on the buttocks. Maternal blood was injected into the patient's buttocks, and she was also given hot and cold tub baths. On the following day the vulva was red, swollen and hot, and there was a swelling of the buttocks at the point where the blood had been injected. A blood count showed 26,000

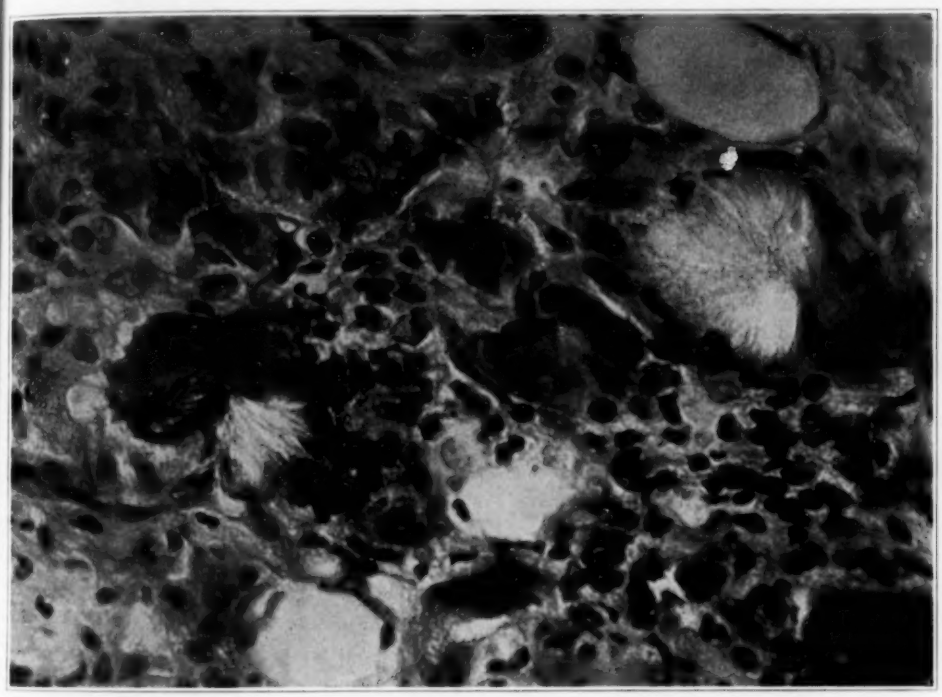


Fig. 1 (case 1).—Details of needle-shaped crystals and foreign body giant cells.

leukocytes with 84 per cent polymorphonuclears. During the first three days the patient lost ½ pound (200 Gm.), became moderately dehydrated and was given physiologic solution of sodium chloride by hypodermoclysis. One week following birth she was in good general condition and gaining in weight. The vulvar lesion had improved, but there were still a few hard, deep-seated lesions. The buttocks were almost normal. At this time a reddish area about 1½ inches (3.8 cm.) in diameter was noted on the back at the level of the ninth dorsal vertebra. Two days later this became purplish and fluctuated. The induration had extended to the shoulders and was described as lobulated, somewhat hard and firmly attached to the skin. On the twelfth day the disease had spread over the upper half of the back, the deltoid region and the medial and lateral aspects of the thighs. There were still indurated areas in the buttocks and vulva.

A small cyst in the center of the large area on the back was aspirated, and about 0.1 cc. of creamy white material was obtained. Microscopic examination revealed fat droplets and crystals. It could not be determined whether these were of neutral fat or fatty acid. They failed to stain with sudan III, and warming did not melt the crystals or increase their staining capacity. No cholesterol

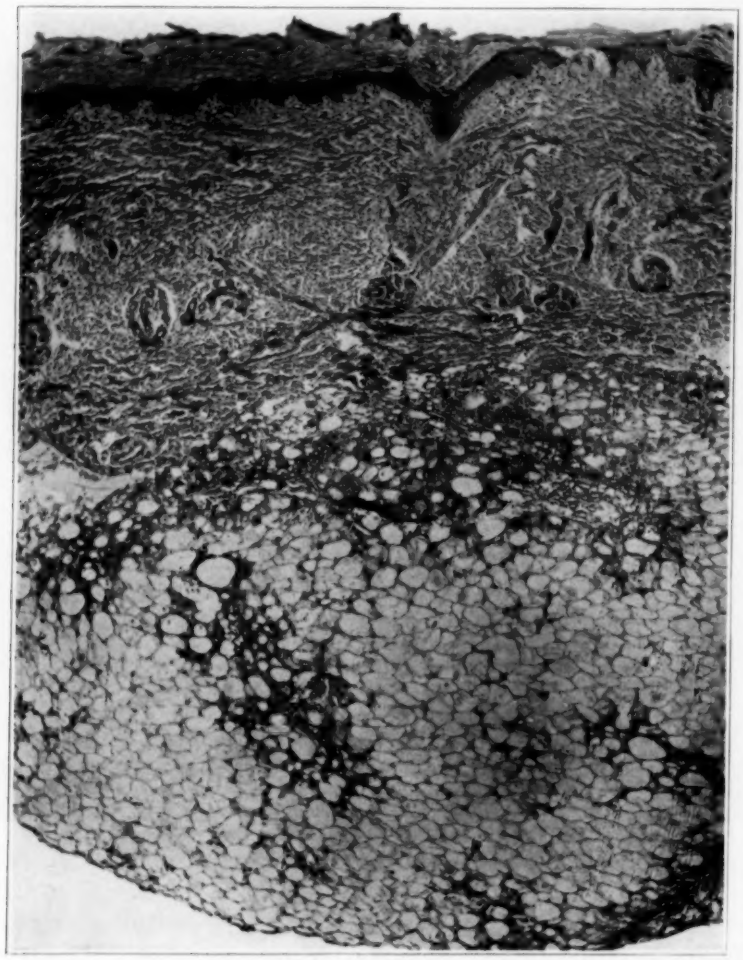


Fig. 2 (case 2).—Low power photomicrograph of areas of fat cell necrosis in the hypoderm, the cutis being normal.

crystals were seen. Negative results were obtained from a roentgenogram to determine the presence of calcium salts. No biopsy was made.

The temperature remained normal except on the third day after birth when it rose to 101 F., owing to a temporary diarrhea. When the patient, 5 weeks old, was last seen on February 10 by a visiting nurse, the lesions had almost entirely disappeared, a few small nodules being present in the middle of the back.

HISTOLOGIC REPORT OF THREE CASES

Biopsies were performed in three cases (1, 2 and 4) under a local anesthetic, the wounds healing by primary union. Paraffin sections were made in all cases and frozen sections in one, and these were stained by hematoxylin and eosin. Histologic examinations were made by Dr. T. J. Riordan, who submitted the following combined report of the three cases, as the changes were essentially the same.

"The epidermis and cutis are either normal or show banal inflammatory changes. The main process involves the hypoderm. The septal bands separating the fat lobules are increased in number, are edematous and well vascularized. These bands and the adjacent fatty tissues are densely infiltrated. Normal fat cells appear as empty spaces. Those which have undergone necrosis are filled with pinkish stained material in which are numerous needle-like crystals (fatty acid?). The blood vessels are dilated, and some are hemorrhagic. The infiltration consists of histiocytes (epithelioid and reticulo-endothelial cells), giant cells of the foreign body type (macrophages), a few fibroblasts and an occasional eosinophil. The giant cells dominate the picture. They are numerous and vary in size, shape and nuclear arrangement. The cytoplasm is foamy and stains bright red with hemotoxylin and eosin. Needle-like crystals are included in many giant cells usually radiating from a pale or clear center. The diagnosis was subcutaneous fat necrosis with granulomatous infiltration predominated by giant cells containing needle-like crystals."

The sections were also examined by Prof. Alexander Fraser, who concurred in the diagnosis.

ETIOLOGY

The most important etiologic factor is generally agreed to be some form of trauma. This was suggested by Cruse and strongly urged by Lieberthal [17] in his presentation before this association in 1918. DeVel and Bolin summarized the action of trauma as (1) an anemia of local areas caused by compression against hard underlying structures during birth and (2) too vigorous methods of resuscitation. Some show other evidences of trauma, such as hematoma, paralysis or intracranial hemorrhage. Furthermore, the lesions of subcutaneous fat necrosis are seen mainly on the exposed parts, such as the cheeks, chin, back, buttocks and deltoid region.

Other arguments in favor of traumatic origin are that similar changes may occur in adults, especially in obese women with large breasts who have been subjected to trauma (Lee and Adair [18] and others). Subcutaneous fat necrosis has also been experimentally produced by Berner [19] and others by traumatization of the skin of young pigs.

---

17. Lieberthal, David: Sclerema Neonatorum and Scleroderma, J. Cutan. Dis. **36**:29, 1918.

18. Lee, B. J., and Adair, F.: Traumatic Fat Necrosis of the Female Breast and Its Differentiation from Carcinoma, Surg., Gynec. & Obst. **34**:521 (April) 1922.

19. Berner, O.: Subkutane Fettgewebsnekrose, Virchows Arch. f. path. Anat. **193**:510, 1908.

Intense cold has been thought to be an additional factor in causing the disease. This was suggested by Cruse and proved experimentally by Lemez. The latter considered that it plays the part of an adjuvant in a marked degree in cases in which cold water is poured on the skin for purposes of resuscitation. Lemez agreed from his experiments and from the observations of others that trauma is the chief cause of the disease. In only rare instances, he thought, can cold be the sole etiologic factor.

While it seems probable that trauma is the main cause of subcutaneous fat necrosis, its mechanism is not yet known. From analogy of pancreatic fat cell necrosis due to a ferment, it has been suggested that subcutaneous fat cell necrosis may also be due to a ferment from leukocytes liberated by trauma (Lecène and Moulonguet). Infiltrating blood in the fat would supposedly supply the fat-dissolving ferment. To meet the objection that there may be no evidence of local hemorrhage, these authors suggest that in certain cases the process may be due to local anemia, which lessens the vitality of the tissues and liberates a tissue ferment.

Though some intensive work has been done on the chemical phase of fat changes, the results seem to be conflicting and have not proved the pathogenesis of the disease. Thus the crystals were thought by Schultz to be composed of a palmatin-stearin mixture. Carol and van der Zande considered them cholesterol esters, Harrison [20] neutral fats, Keilmann, Smith and others fatty acids and Lecène and Moulonguet [21] soaps. From his studies, Harrison concluded that the disease is a primary inflammation of the subcutaneous tissues of unknown cause. Gray stated the opinion that it is possible that the fat cells are damaged by some toxic influence.

DIFFERENTIAL DIAGNOSIS

Sclerema Adiposum (Sclerema Neonatorum).—Unlike subcutaneous fat necrosis which usually affects large and otherwise normal babies, sclerema adiposum is chiefly seen in undernourished, debilitated and premature infants. It may appear suddenly on the third or fourth day or any time during the first weeks of life, without apparent cause except undernourishment and debility, or at a later age in babies with gastro-intestinal disorders, especially severe diarrhea, resulting in dehydration. The lesions appear first on the lower extremities, usually on the calves, and extend upward rapidly. They may involve the entire surface, with the exception of the palms, soles and scrotum. The

20. Harrison, G. A.: An Investigation of Sclerema Neonatorum with Special Reference to the Chemistry of the Subcutaneous Tissues, Arch. Dis. Childhood **1**:123, 1926.

21. Lecène and Moulonguet: La cystosteatonécrose ou saponification intracellulaire du tissu cellulo-adipeux sous-cutane, Ann. d'anat. path. **2**:193 (May) 1925.

skin, instead of being apparently swollen and reddish as in fat necrosis, is shrunken, smooth, has a whitish or waxy color and is cold to the touch, the temperature being nearly always markedly subnormal. As in fat necrosis, the indurated areas are extremely hard and do not pit on firm pressure. In the severest cases the infants are unable to move; the pulse and respiration become increasingly slower, and the appearance of a frozen cadaver is simulated. The disease is fatal in the great majority of cases, the duration being only a few days as a rule.

From the foregoing brief description it would appear that sclerema adiposum can, as a rule, be clinically differentiated from subcutaneous fat necrosis. Sclerema adiposum is, incidentally, a much rarer disease than subcutaneous fat necrosis.

Pathologically, the changes in sclerema adiposum consist in a stearin-like hardness of the fatty tissue combined with a marked dehydration of the skin and subcutaneous tissue. On cutting the tissue, there is practically no escape of fluid.

The two diseases can also apparently be differentiated histologically, though few examinations of this kind are recorded in the literature. In the cases of Luithlen [22] and Mensi,[23] numerous fat crystals were present in the fatty tissue but no changes were noted suggesting necrosis or an infiltrating granuloma. A typical case of what I think should be classed as sclerema adiposum as opposed to subcutaneous fat necrosis is reported by Gray. This was in an infant born after normal labor, with marked dehydration following diarrhea for three days, in whom boardlike hardness of the subcutaneous tissues developed two days before death. On histologic examination no fat crystals were observed, and the "sections differed very little from those of normal fat." Chemical examinations showed that the melting point of the fat was only slightly above normal. Gray said: "It is possible that it was to this type of case that the name sclerema was first applied," and suggested that the term "acute sclerema" might be appropriate for these cases.

In this brief publication I shall not attempt to discuss the pathogenesis of sclerema adiposum, about which opinions have differed greatly. I should merely say that obstetric trauma does not seem to be a factor, as so many of the patients are premature or small-sized infants. It appears that loss of body fluids (dehydration) at least plays an important etiologic rôle.

Sclerema Edematosum.—This condition usually called edema neonatorum in this country, is a rare disease which was formerly confused with sclerema adiposum. It usually begins on from the second to the

22. Luithlen, F.: Die Zellgewebsverharterungen der Neugeborenen, Vienna, Alfred Hölder, 1902.

23. Mensi, E.: Sulle alterazioni cutanee dello sclerema, Gior. ital. d. mal. ven., Milano **53**:209, 1912.

fourth day of life and is chiefly seen in weak and premature infants and often in twins. It begins as an edematous swelling of the dorsal surface of the feet, calves, thighs, mons veneris and also of the upper extremities and eyelids. Some cases are extensive, while others are less so and involve only favorite sites, especially the feet. There may be a reddish color at first and often a light yellowish hue from accompanying jaundice. The temperature is usually low, but not as low as in sclerema adiposum. The disease is usually fatal in from four to five days, although some patients with mild cases recover.

The most important clinical features that differentiate this disease from subcutaneous fat necrosis are that there are never any sharply circumscribed isolated lesions, and that the affected areas show a characteristic pitting on pressure which is slow to disappear. In severe cases there is said to be an elastic feeling on palpation.

Few histologic examinations have been made, and these have shown intense edema and noncharacteristic inflammatory changes in the skin, the subcutaneous tissues and even the underlying muscles. Mensi found a hemorrhagic infiltration in the subcutaneous tissue, the fat being otherwise normal. On histologic examination, there could be no possibility of mistaking this disease for subcutaneous fat necrosis.

Many theories have been suggested for its causation, including the one that it is due to syphilis, jaundice or various infections. Such cases are classed by Luithlen as symptomatic. In other so-called idiopathic cases, the causation is open to speculation. Cold has been considered to be an exciting factor.

Scleroderma.—Scleroderma of new-born infants has been confused with subcutaneous fat necrosis until recent years when the differentiation became possible through histologic examination. It has been shown by this means that scleroderma of the new-born is an exceedingly rare disease. Diss and Woringer [24] expressed the belief that only three of the recorded cases should be accepted as true scleroderma, including those of Cockayne,[25] Kneschke [26] and Löwenberg.[27] To these Lemez would add the cases of Kraus [28] and Cavenenghi.[29] Weidman's [30] case,

24. Diss, A., and Woringer, F.: Les fausses sclérodermies du nourrisson, Bull. Soc. franç. de dermat. et syph. **36**:960, 1929.

25. Cockayne, E. A.: Congenital Sclerodermia and Sclerodactylia, Proc. Roy. Soc. Med. **9**:62 (March) 1916.

26. Kneschke, W.: Sclerodermie im Säuglingsalter, Arch. f. Dermat. u. Syph. **146**:105 (July) 1923.

27. Löwenberg, R. D.: Zur angeborenen diffusen Sklerodermie, Dermat. Wchnschr. **79**:893 (Aug. 2) 1924.

28. Kraus, A.: Beitrag zur Klinik und Anatomie der Sclerodermie im Kindesalter, Med. Klin. **21**:935 (June 25) 1925.

29. Cavanenghi, G.: Un caso di sclerema congenito, Studi sassaresi **3**:582, 1925.

30. Weidman, F. D.: Necropsy Findings in a Case of Congenital Scleroderma and Sclerodactylia, Arch. Dermat. & Syph. **1**:375 (April) 1920.

according to these authors, should be placed in a separate category. It showed a generalized fibrosis, including internal organs such as the liver and pancreas, and was probably a result of syphilis, the infant dying of enteritis and meningitis. Histologic examination in the cases of Kneschke, of Löwenberg and of Kraus showed lesions in the cutis similar to those of scleroderma of adults, with no abnormal change in the fatty tissue.

While certain diagnosis in early infancy could be made only by histologic examination, it might also be surmised by the course of the disease in infants who survive. If the process continued unchanged during a year or more, a diagnosis of scleroderma would be justified. It would certainly exclude the consideration of subcutaneous fat necrosis, which disappears completely within a few months.

The case of Cockayne was reported a second time when the patient was 2 years old. At that time there had been little change in the disease. There were well marked lesions of the forearms, hands and legs below the knees. It was also stated that the "skin of the abdomen was sclerodermatous and pigmented," this being a region, incidentally, in which subcutaneous fat necrosis has not as yet been observed. The patient also suffered from hydrocephalus and nail deficiency and had no teeth. Knescke's patient was seen two years later by Galewsky,[31] who observed decided evidence of generalized scleroderma, while the case reported by Kraus was under his observation when the patient was nearly 7 years old, and, although there had been partial involution, the cutaneous changes in the lower extremities were still pronounced.

There can be little doubt that many cases described in the literature as scleroderma prior to a dozen years ago were improperly labeled. Luithlen in his excellent monograph quoted five English cases reported as cases of sclerema neonatorum in which, he argued, this disease (meaning sclerema adiposum) was not present, the condition, in his opinion, being scleroderma. In view of present knowledge, I should call them classic examples of subcutaneous fat necrosis. The same could be said of the case recorded by Lieberthal as scleroderma neonatorum. No histologic examination was made in this case; the infant was otherwise normal and made a complete recovery within nine weeks. At the time of Lieberthal's publication (1918), very little was known of subcutaneous fat necrosis. In view of the rapid recovery, it must have been presumed that scleroderma in new-born infants was a strikingly mild disease and ran an entirely different course from that of adults.

---

31. Galewsky, E.: Ueber kindliche Sklerodermie, Zentralbl. f. Haut.- u. Geschlechtskr. **15**:413 (June 29) 1924.

SUMMARY

Five cases of subcutaneous fat necrosis of the new-born are reported, four of them being in girls. All of the babies were born at full term and were of good size. Three of the mothers were primiparas. Evidence of trauma, due to delivery or methods of resuscitation was present in four cases. The disease was extensive in three cases, occupying the greater part of the back, buttocks and posterior surface of the lower extremities. It was less extensive in the other cases. The lesions were strikingly similar in all, varying from small nodules to extensive areas, which were bluish red at the outset, hard, painless, not pitting on pressure and fairly well defined. The lesions were first noticed at birth or within two to three weeks thereafter. Complete recovery occurred within two to three months in three cases. In one case the lesions had almost disappeared at the end of five weeks, and in another they were undergoing involution at the end of six weeks. Two cases showed small cysts from which whitish, creamy material was evacuated showing needle-shaped crystals. Roentgen examinations to show the possible presence of lime salts gave negative results in two cases. In a third case irregular density of the soft tissues was noted, but was not considered diagnostic. The general health was good in all cases and a steady gain in weight was recorded. Histologic examinations were made in three cases and showed strikingly similar changes in the subcutaneous tissue, with negative or unimportant alterations in the cutis. The essential process consisted of necrosis of subcutaneous fat cells with a granulomatous infiltration, in which giant cells predominated, containing needle-like crystals.

CONCLUSIONS

1. Subcutaneous fat necrosis is a definite, benign, self-limited disease of new-born or young infants.

2. It can be differentiated as a rule from sclerema adiposum, sclerema edematosum and scleroderma.

3. The term subcutaneous fat necrosis is suitable in view of the histologic changes. It is preferable to the term sclerema, which causes confusion.

4. Trauma during delivery or subsequently from methods of resuscitation is an important etiologic factor.

5. The generalized type of scleroderma in the new-born is an exceedingly rare disease and can be easily differentiated from subcutaneous fat necrosis by histologic examination or the subsequent course of the disease in infants who survive.

6. The reports of many cases of sclerema and scleroderma in the literature prior to the last decade must be reconsidered in view of present knowledge of subcutaneous fat necrosis.

ABSTRACT OF DISCUSSION

DR. V. PARDO-CASTELLO, Havana, Cuba: I wish to subscribe to everything Dr. Fox has said. It was my good fortune to see a case of sclerema neonatorum several years ago. It was a severe case, and the child died in a short time. When I saw the patient she was about 10 days old, and I found the hard edematous appearance and the waxy color up to the groins. The condition gradually invaded the abdomen and chest, and the child promptly died.

Another case seen by me was one of the localized type Dr. Fox described. That patient recovered. We had another case in our clinic which was diagnosed as scleroderma and which was very difficult to differentiate from sclerema neonatorum. In cases of generalized sclerema, the child seems to be in great distress, which is not the case with the localized lesions. The cases of generalized sclerema neonatorum are very severe, and the children die quickly.

DR. FRED WISE, New York: I am free to admit that we sometimes encounter cases in our clinic, referred by the pediatric department, in which we are unable to offer a logical diagnosis, and also that we have made mistakes at times and have been unable to inform the consulting pediatrician as to the correct clinical interpretation of the child's lesions. We knew only that we were not dealing with true scleroderma. Dr. Fox's paper has opened my eyes to the fact that we were confronted with one of three diseases, and the probability is that some of the cases seen even in the last year were examples of fat necrosis.

One of the things that interests me in connection with the paper is the relation between these cases of fat necrosis and the instance described fifteen years or so ago by Gilchrist and Ketron as fat necrosis in an adult, and those in which there was a similar histologic appearance in patients described by Parkes Weber of London and by Christian of Boston. They reported examples in adults, associated with fever, which persisted for long periods but did not directly cause death. If I remember correctly, the changes in the tissue in the cases described by Gilchrist and by Christian were similar to those now described by Fox.

DR. FRED D. WEIDMAN, Philadelphia: I have had three laboratory experiences with these hard-skinned babies. Dr. Fox referred to the one case of scleroderma which has been published. Of the other two cases, one was presented at our local dermatological society by Dr. Patricia Drant as sclerema neonatorum. We studied the sections together, and the findings were identical with those Dr. Fox showed today on the screen. On investigation we eventually found that this condition had been described previously as lipophagic granuloma. Dr. Drant then reproduced the lesion in young mice, and since her patient had been born in difficult labor and had been forcibly slapped in efforts at resuscitation, she practiced trauma on the mice. Some were forcibly pinched, and in others substances were injected subcutaneously, such as hot water, xylene and pancreatic extract. The disease developed only in the rats that had been traumatized; at least the histologic pictures of these animals were identical with those of the infants. The experiments were repeated on hogs and were unsuccessful, probably because the animals were too old. We were unaware at that time of the experiments on hogs that Dr. Fox has reported this afternoon.

The questions brought up are these: Why is it that in younger animals one finds this sort of change, whereas in older animals it does not occur? Why is it that in some of the babies one finds fat granulomas, but in most one does not? I wonder whether there is not something in the fat metabolism of these children that may explain the situation. Dr. Fox told us how robust these infants are, just as in xanthoma tuberosum we see subjects who are robust. I think that one of the inquiries we should prosecute in future investigations concerns blood cholesterol

and other values not only of the babies but of the mothers (composition of milk). It may be that slapping the normal fat of babies is not sufficient to produce this condition because the fat can be absorbed, while in abnormally constituted fatty tissues the fats are in effect foreign bodies and promote this reaction.

Regarding the particular designation we give the condition, no doubt some of the cases are cases of fat necrosis from the first. I think it is still possible that some of them need never have shown true fat necrosis. Necrosis means death. In the sections I studied and in the illustrations shown by Dr. Fox there were no evidences of necrosis. Dr. Fox told me that in some cases reported in the literature there were such findings. Many of the infants may have had abnormally constituted fat substances in the subcutaneous tissue without proceeding as far as fat necrosis. I think that the better name is lipophagic granuloma.

Dr. Harry E. Alderson, San Francisco: The histologic picture shown by Dr. Fox is quite similar to that seen in a case of panniculitis which I am going to report later. Could this be a similar disease? Since these infants recovered and practically all the cases of relapsing panniculitis occur in obese women past the menopause, I wonder whether or not it is worth while to consider the following possibility. Could the infants' natural recuperative ability be the factor that brings about recovery? Could failure to recover in the cases of adult panniculitis be due to the naturally low resistance that is often present after the menopause?

Dr. Howard Fox, New York: As to the use of roentgenotherapy in these cases, I think that the value of such treatment would be hard to prove. If the patients do not die of intercurrent disease, they invariably get well spontaneously.

In regard to differentiating these cases from myositis, I think that could be done by the absence of pain. These lesions are hard and apparently painless.

I appreciated the suggestions of Dr. Weidman and Dr. Alderson. Though my associates and I feel that we have a rather good idea of the etiology of the disease, its histogenesis is unknown.

I agree that the name lipophagic granuloma is a suitable term, for that is what strikes one immediately on looking at the histologic specimens. My purpose has been to bring this subject to the attention of the association and to show that this particular class of cases can be distinguished from sclerema and from scleroderma of the new-born.

Dr. George M. MacKee: What is the etiology of the condition?

Dr. Howard Fox: The most important etiologic factor appears to be trauma during birth or from overzealous methods of resuscitation. The babies are often of large size, and labor is frequently prolonged or forceps are used. As a result of trauma, there is necrosis of the subcutaneous fat, with the formation of a foreign body granuloma. In a few months there is a complete return to the normal condition. I shall not discuss this at length, as it is the subject of a paper to be read soon at the American Dermatological Association. I shall merely say that this is the third such case that I have reported before dermatologic societies, and the fifth that I have observed. The patient whom I presented four years ago before this society was seen recently, and was a vigorous healthy child. Three other conditions must be considered in the differential diagnosis: sclerema adiposum (sclerema neonatorum), sclerema edematosum and scleroderma.

EXFOLIATIVE DERMATOSIS AND MALIGNANT ERYTHRODERMA

THE VALUE AND LIMITATIONS OF HISTOPATHOLOGIC STUDIES

HAMILTON MONTGOMERY, M.D.
ROCHESTER, MINN.

I propose to consider the value and limitations of histopathologic studies as an aid in the diagnosis of seventy-three cases of exfoliative dermatitis and sixteen cases of generalized erythroderma. The study includes cases of exfoliative dermatitis of the primary or idiopathic type (Wilson) and cases secondary to various types of dermatosis, such as psoriasis, eczema, seborrheic dermatitis, lichen planus and the administration of drugs, particularly arsenic. The study will also include cases of exfoliative dermatitis and erythroderma associated with the different manifestations of lymphoblastoma, which include mycosis fungoides, leukemia cutis, Hodgkin's disease and lymphosarcoma. The term "malignant erythroderma" is used to designate a generalized or universal erythrodermatous phase of any of the types of lymphoblastoma, in which the clinical picture is not diagnostic and in which insufficient scaling is present to justify the term exfoliative dermatitis. When a patient presents either universal erythroderma or exfoliative dermatitis, the clinical features of the disease in question are frequently so obscured as to make definite diagnosis impossible on the basis of objective examination only. In this series it frequently was necessary to employ all the diagnostic measures available, including careful clinical examination; taking of a history; roentgenologic examination; studies of the blood, especially the differential count, and other cytologic studies; search for heavy metals in the urine, hair and other tissues, and biopsy not only of the skin, but often of the lymph nodes as well. Even then prolonged observation and repeated studies may be required to establish the diagnosis. Arzt and Fuchs [1] stated that in rare instances the diagnosis may remain indeterminate even after postmortem examination has been made. In this paper no attempt will be made to describe in detail all the histopathologic changes seen in any

From the Section on Dermatology and Syphilology, the Mayo Clinic.

Read before the Fifty-Fifth Annual Meeting of the American Dermatological Association, Havana, Cuba, May 5, 1932.

1. Arzt, L., and Fuchs, H.: Hauterkrankungen bei Leukosen und Leukoblastomen sowie verwandten Zuständen, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1929, vol. 8, p. 1.

or all of the types of dermatosis in question; rather the differential diagnostic histopathologic features in this group of cases with exfoliative reactions will be emphasized. The histologic features will be considered in two parts: the first will be concerned with exfoliative dermatitis resulting from psoriasis, hereafter called erythroderma psoriaticum, and the means of distinguishing it from other forms of exfoliative dermatosis; the second, with forms of exfoliative dermatosis and of malignant erythroderma in their relationship to lymphoblastoma. Many patients in the first or benign group responded to

TABLE 1.—*Classification of Seventy-Three Cases of Exfoliative Dermatitis (Based on Correlation of Histopathologic with Clinical and Various Laboratory Features)*

Type or Predominant Etiologic Factor	Cases	Percentage of 73 Cases
Lymphoblastoma	18	24.6
Psoriasis	14	19.3
Eczema (including 1 case of infantile eczema and 5 cases of so-called allergic type of eczema)	15	20.5
Arsenic and eczema	5	6.8
Arsenic only (1 case due to arsphenamine; 1 case due to arsenic spray)	2	2.7
Lead (including paint)	3	4.1
Gold treatment (for lupus erythematosus)	1	1.4
Seborrheic dermatitis	2	2.7
Lichen planus	2	2.7
Toxic	2	2.7
Dermatitis exfoliativa neonatorum (Ritter)	1	1.4
Ichthyosiform erythroderma	1	1.4
Etiology indeterminate	7	9.6

TABLE 2.—*Lymphoblastoma* (Based on Biopsy of Skin Correlated with Clinical Findings)*

Type	Cases	Percentage of 34 Cases
Mycosis fungoides	5	14.7
Leukemia cutis (lymphatic)	4	11.7
Leukemia cutis (myelogenous)	1	3.0
Hodgkin's disease	1	3.0
Lymphosarcoma	4	11.7
Lymphoblastoma (type indeterminate)	19	55.9

* Eighteen cases of exfoliative dermatitis and 16 cases of malignant erythroderma.

treatment; in the second group (lymphoblastoma) many died at home; necropsy was not performed. Some patients have been seen too recently to allow a final opinion to be expressed. Postmortem examination has been performed in only six cases, either at the Mayo Clinic or elsewhere. Tables 1 and 2 represent a classification of the types of exfoliative dermatosis based on correlation of the histologic, clinical and laboratory data.

The histopathologic picture of exfoliative dermatosis that is the result of extension of a localized disease is essentially that of the localized disease. Even when the disease apparently starts as exfoliative dermatitis, it nevertheless retains histopathologic features of the

localized form. The following cases of localized disease, therefore, were also studied: sixty-one cases of lymphoblastoma; forty cases each of psoriasis and lichen planus; more than sixty cases of eczema of various types; twenty-six cases of dermatitis or pigmentation due to arsenic; sixteen cases of parapsoriasis of various types; ten cases of neurodermatitis; several cases of pityriasis rubra pilaris (Devergie), dermatitis medicamentosa (other than arsenic), seborrheic dermatitis and pityriasis rosea, and one case of acrodermatitis continué of Hallopeau. The number of cases was more than three hundred and fifty, and more than ten times that number of slides were examined. Serial sections were made in some of the cases, and various stains were used.

It seems advisable, in procuring a specimen for biopsy in cases of exfoliative dermatosis, no matter what the cause, to select an area that has not been subject to recent treatment, to avoid the so-called seborrheic areas, for the majority of patients present a varying amount of seborrhea which may confuse the issue, and to sterilize the area from which the specimen is to be taken by the application of alcohol rather than by vigorous scrubbing with soap and water, which may remove several of the diagnostic features in the disease concerned. Specimens for biopsy should not be taken from the abdomen, because atrophy of the skin resulting from striae cutis distensae may confuse the issue. An obvious, yet not often considered, factor is that a biopsy for diagnosis should not be made from an involuting lesion. The question as to the site and technic of biopsy is covered in the recent article by Jacob and Helmbold [2] and the discussion of it.

EXFOLIATIVE DERMATITIS DUE TO PSORIASIS (ERYTHRODERMA PSORIATICUM)

Gans [3] called to my attention the value of histopathologic studies in the exfoliative types of dermatosis, especially in regard to the diagnosis of erythroderma psoriaticum. Goeckerman and O'Leary [4] reported that patients with erythroderma psoriaticum responded to treatment with crude coal tar and ultraviolet light almost as promptly as patients with psoriasis vulgaris. Since 1927, I have made a histopathologic diagnosis of psoriasis in fifteen cases of exfoliative dermatitis in which the patients came under the care of the physicians in the Section on Dermatology and Syphilology at the Mayo Clinic. In ten of the cases the

2. Jacob, F. M., and Helmbold, T. R.: Indications for and Limitations of Biopsy in About Five Hundred Dermatologic Cases, J. A. M. A. **97**:987 (Oct. 3) 1931.

3. Gans, Oscar: Personal communication to the author.

4. Goeckerman, W. H., and O'Leary, P. A.: Erythroderma Psoriaticum: A Review of Twenty-Two Cases, J. A. M. A. **99**:2102 (Dec. 17) 1932.

histopathologic picture was typical; in four it was suggestive, and further observation of these four cases proved them definitely to be of psoriatic origin; in one case the findings were of doubtful significance. This case did not respond to the regimen for psoriasis, and on further observation it was classified as dermatitis exfoliativa of idiopathic type. In six of the fourteen proved cases of erythroderma psoriaticum, diagnosis by clinical means was not possible, but was established by the histologic findings; in the other eight cases, the histopathologic findings were of definite value in confirming the clinical diagnosis.

The histopathologic changes in psoriasis, from the earlier stages through to the end-stages, were carefully analyzed by Gans [5] and Nobl,[6] and especially by Haslund.[7] Mention must also be made of articles by Heimann [8] and Civatte,[9] and of the excellent summary in Darier's [10] "Précis de dermatologie." With the views of these authors, I am, in the main, in entire accord. On the basis of a detailed histopathologic study of fifty-four cases of psoriasis, including the fourteen cases of erythroderma psoriaticum, I cannot agree with Kyrle [11] regarding the relationship of psoriasis to varicella or to Guarnieri-like bodies. The cardinal histopathologic features, or perhaps I may say diagnostic features, of psoriasis are a combination of the following: uniform parakeratosis; regular acanthosis with mild intracellular and slight intercellular edema, and with scattered mitosis of the basal and prickle cells; papillomatosis, the papillary bodies frequently reaching to the zone of parakeratosis; clubbing of the papillary bodies; dilatation and tortuosity of the loops of the capillary vessels, and, in the upper part of the cutis, mild perivascular infiltration of polymorphonuclear leukocytes and lymphocytes (figs. 1 and 2). Migration of leukocytes and lymphocytes through the epidermis, to form the so-called micro-abscesses of Munro, confirms the diagnosis, but is not essential to establish such a

5. Gans, Oscar: Psoriasis, in Histologie der Hautkrankheiten, Berlin, Julius Springer, 1925, vol. 1, p. 280.

6. Nobl, Gabor: Psoriasis, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol. 7, p. 180.

7. Haslund, P.: Die Histologie und Pathogenese der Psoriasis, Arch. f. Dermat. u. Syph. **114**:427 and 745, 1913.

8. Heimann, W. J.: Histopathology: III. Scaling Inflammations of the Psoriasiform Type, J. Cutan. Dis. **34**:202 (March) 1916.

9. Civatte, A.: Psoriasis and Seborrhoeic Eczema: Pathological Anatomy and Diagnostic Histology of the Two Dermatoses, Brit. J. Dermat. **36**:451 (Nov.) 1924.

10. Darier, Jean: Précis de dermatologie, ed. 4, Paris, Masson & Cie, 1928, p. 125.

11. Kyrle, Josef: Vorlesungen über Histo-biologie der menschlichen Haut und ihrer Erkrankungen, Berlin, Julius Springer, 1925, vol. 1, p. 169; 1927, vol. 2, p. 266.

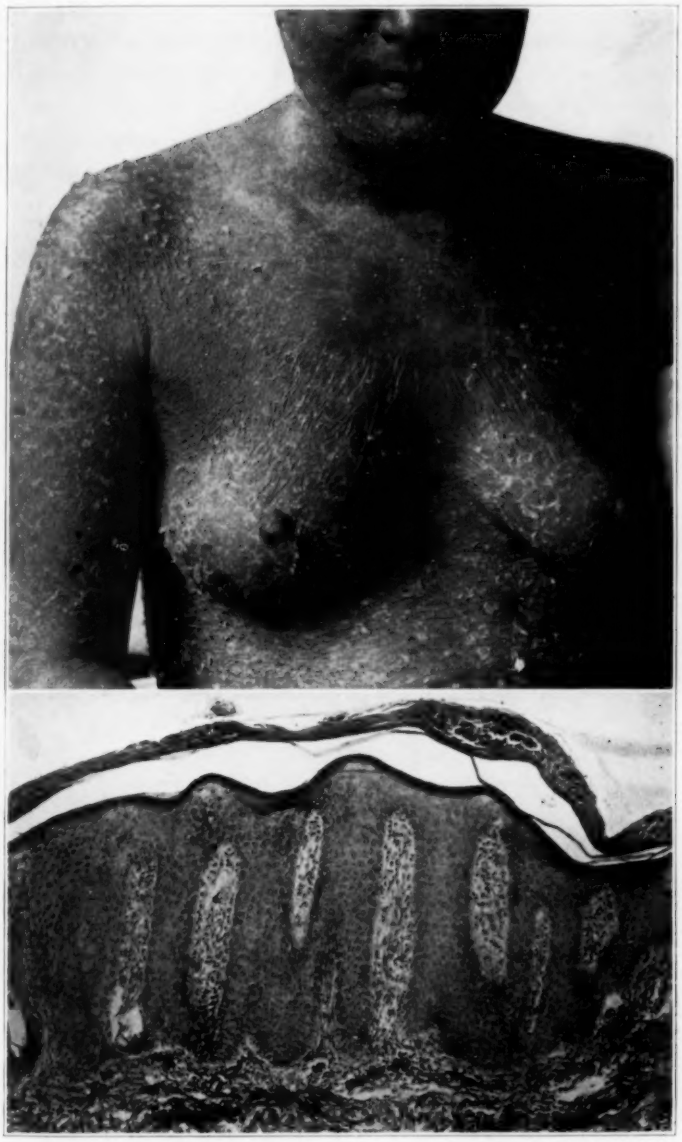


Fig. 1.—Erythroderma psoriaticum. Typical histopathologic picture: micro-abscess, regular acanthosis and papillomatosis, dilatation and tortuosity of capillary vessels (× 80).

diagnosis. The histopathologic picture seen in erythroderma psoriaticum differs from that of psoriasis vulgaris only in that more marked intercellular edema may be seen in the epidermis, and that, as a result of this, the superficial layers of the epidermis, containing the micro-abscesses, may be removed through too vigorous scrubbing of the area preparatory to biopsy.

The histologic distinction between psoriasis and other forms of dermatosis involves consideration of a number of diseases. Only the

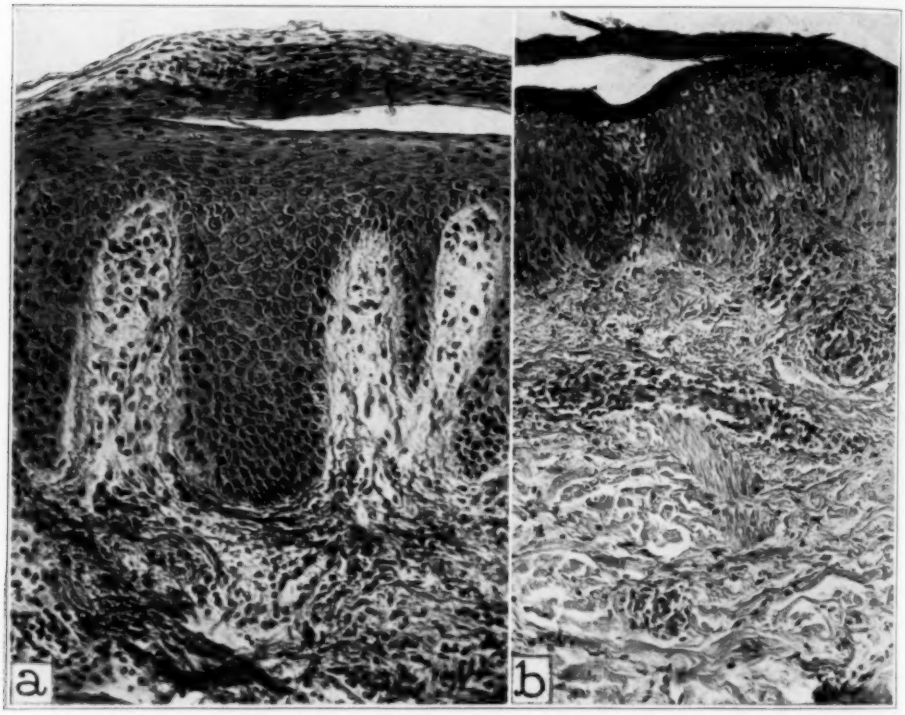


Fig. 2.—In *a*, erythroderma psoriaticum, presenting all the diagnostic features of psoriasis vulgaris, namely, micro-abscess, parakeratosis, regular acanthosis and papillomatosis, clubbing of papillary bodies, dilatation of the capillaries, and sparse infiltrate in the cutis (× 150); in *b*, dermatitis exfoliativa (arsphenamine). Pyknosis and palisade-like arrangement of the basal cells are evident (hematoxylin and eosin; × 125).

following, however, need be considered in distinguishing between erythroderma psoriaticum and other types of exfoliative dermatosis. Eczema, used in the broad sense of the term, whether acute or chronic, is characterized by parakeratosis, hyperkeratosis, acanthosis and spongiosis, with or without the formation of vesicles (fig. 3). Parakeratosis is usually spotted, and rarely assumes the uniform character

throughout the section that is seen in psoriasis. A varying degree of spongiosis is almost always to be found in one or more areas in the same section. The formation of vesicles or pustules usually can be distinguished from the micro-abscess of Munro. Papillomatosis and migration of leukocytes through the epidermis may be seen in both psoriasis and eczema. Mitotic figures in the epidermis are rarely seen in eczema, but are a frequent occurrence in psoriasis. The histologic characteristics of infantile eczema do not differ essentially from those of the adult type. It is usually relatively easy, therefore, to distinguish

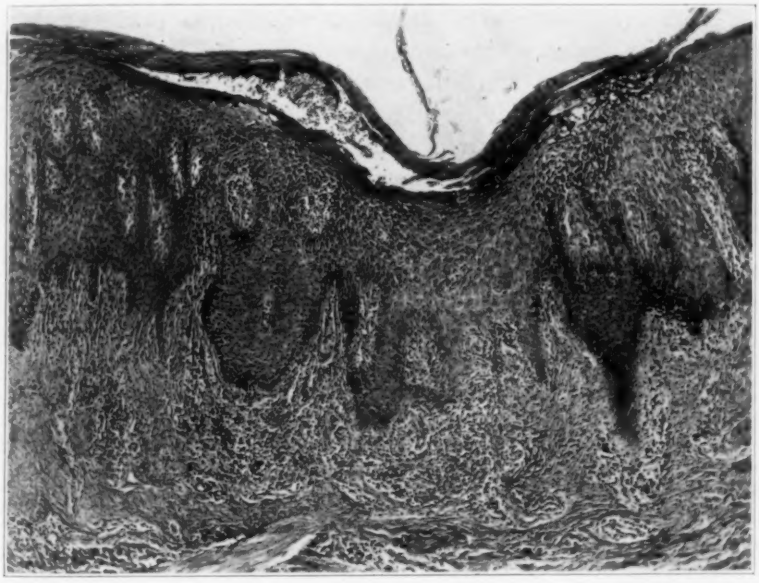


Fig. 3.—Dermatitis exfoliativa. Eczema. Typical picture: parakeratosis, formation of vesicle, spongiosis, acanthosis and moderate degree of infiltrate in cutis (× 65).

histopathologically between exfoliative dermatitis due to eczema and that due to psoriasis.

The distinction between erythroderma psoriaticum and exfoliative dermatitis secondary to seborrheic dermatitis is more difficult. The latter may simulate the histologic picture, either of psoriasis or of eczema. Frozen sections stained for fat may be necessary to settle the question. Seborrheic dermatitis may present uniform parakeratosis, acanthosis and papillomatosis as seen in psoriasis, and even areas suggestive of micro-abscesses. Atrophic changes in the hair follicles may be seen in both conditions. Usually, however, seborrheic dermatitis presents definite areas of spongiosis which distinguish it from psoriasis.

Dermatitis exfoliativa may develop either as the result of the use of arsenic externally or as the result of intravenous administration or ingestion of the drug. The histopathologic picture is often indistinguishable from that of eczema. Frequently, however, and especially in the stages of involution, many of the changes that O'Leary and I [12] have emphasized regarding arsenical pigmentation are present (fig. 2*b*). These consist of relative and absolute hyperkeratosis, relative or absolute atrophy of the prickle cell layer, pyknosis and pallisade-like arrangement of the basal cells, spotted melanin pigmentation of the epidermis and chromatophores laden with pigment in the upper part of the cutis; also, there are dilatation of the blood vessels and mild perivascular infiltration in the same regions. Unless the changes just mentioned are present, demonstration of arsenic in the tissues, by Osborne's method, does not establish the diagnosis, for many patients with exfoliative dermatosis have received arsenic in one form or another as a therapeutic measure. In several cases in which erythroderma psoriaticum developed following the injudicious use of arsenic in the treatment of psoriasis vulgaris, the histopathologic picture was that of psoriasis rather than that of arsenical dermatitis or pigmentation. Exfoliative dermatitis due to any of the other metals may assume the histopathologic features of eczema, plus the special histopathologic and other laboratory evidence of the effect of the metal in question. Dermatitis medicamentosa (except that due to iodides and bromides) frequently presents a picture simulating that seen in erythema multiforme, which is readily distinguished from that of psoriasis. In generalized or universal lichen planus the characteristic histopathologic picture seen in the nonexfoliative stage is to be found. The same is true regarding the histopathologic changes seen in pityriasis rubra pilaris (Devergie). Parapsoriasis is distinguished both by the absence of the characteristic micro-abscesses and by the absence of the combination of the other histopathologic findings seen in psoriasis. Idiopathic dermatitis exfoliativa may also present many of the features of psoriasis, but usually presents areas of spongiosis suggesting eczema. It lacks a specific or characteristic histopathologic picture. A review of the histopathologic changes in dermatitis exfoliativa neonatorum, or of the epidemic form of Savill, is scarcely necessary, for these conditions are readily distinguished by their history.

I have avoided the use of the term "pityriasis rubra of Hebra" because I am in entire agreement with Barney [13] regarding abandon-

12. Montgomery, Hamilton, and O'Leary, P. A.: Pigmentation of the Skin in Addison's Disease, Acanthosis Nigricans and Hemochromatosis, Arch. Dermat. & Syph. **21**:970 (June) 1930.

13. Barney, R. E.: Pityriasis Rubra (Hebra), Arch. Dermat. & Syph. **18**:716 (Nov.) 1928.

ment of this term. Tuberculosis has been reported as the etiologic factor in some cases of exfoliative dermatitis. In only one case of exfoliative dermatitis in this series was evidence of active tuberculosis presented. This patient had chronic tuberculous pleurisy, which apparently was not a causative or even a contributory factor in the production of the dermatitis. On the other hand, in at least two of the cases of lymphoblastoma with exfoliative reactions the clinical picture was consistent with the diagnosis of pityriasis rubra of Hebra.

LYMPHOBLASTOMA, ESPECIALLY IN REGARD TO EXFOLIATIVE DERMATITIS AND MALIGNANT ERYTHRODERMA

The types of exfoliative dermatosis considered so far usually can be distinguished histologically from lymphoblastomatous involvement, because in the former the amount of infiltrate in the cutis is smaller than in the latter, and also because the character of the infiltrate in the former differs from that in the latter. It is important, however, to recognize that exfoliative dermatitis of an inflammatory or idiopathic type may, in rare instances, represent an early, nonspecific stage, or a toxic reaction, of one of the types of lymphoblastoma.

I am in accord with those authors who believe that there is a close relationship between mycosis fungoides, leukemia cutis, Hodgkin's disease and lymphosarcoma, but I think that until more is known regarding the etiology of the different diseases concerned, the attempt should still be made to classify them as separate but related entities. The literature and various points of view regarding the diseases mentioned are fully covered by Arzt and Fuchs, Herxheimer and Martin [14] and Schoenhof.[15] Erythroderma and exfoliative dermatosis are reviewed by Juliusberg.[16] The histopathologic changes are fully considered by Gans,[17] Kyrle and McCarthy.[18] The concept of lymphoblastoma, pro-

14. Herxheimer, K., and Martin, H.: Mycosis Fungoides, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1929, vol. 8, p. 174.

15. Schoenhof, Siegmond: Die Lymphogranulomatose der Haut, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1929, vol. 8, p. 271.

16. Juliusberg, Fritz: Die psoriasiformen, pityriasiformen, exfoliativen Erythrodermien, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol. 7, p. 289.

17. Gans, Oscar: Histologie der Hautkrankheiten, Berlin, Julius Springer, 1925, vol. 1, p. 557; The Skin Picture in Hematopoietic Diseases, Arch. Dermat. & Syph. **16**:1 (July) 1927.

18. McCarthy, Lee: Histopathology of Skin Diseases, St. Louis, C. V. Mosby Company, 1931, pp. 283 and 483.

mulgated by Warthin [19] and Mallory,[20] has been elaborated on in regard to cutaneous manifestations in recent articles by Cole,[21] Fox,[22] Fraser,[23] Keim,[24] Ketron and Gay,[25] Miller,[26] Symmers,[27] Wile,[28] Wise [29] and others.

I shall first give the histologic criteria for the diagnosis of the different types of lymphoblastoma, and later consider the histopathologic changes seen in the exfoliative and generalized erythrodermatous phase of these diseases. I recognize that in some cases the patient may present the clinical and histologic features of one disease, only subsequently to develop those of another disease in this group. The following criteria are based on an analysis of a total of ninety-five cases of lymphoblastoma of the skin, together with a review of the literature.

Mycosis fungoides may be divided into an eczematoid or premycotic stage, an infiltrative stage and a stage of tumor. In the earliest or premycotic stage, the histopathologic picture may be nonspecific, and the changes may resemble those seen in eczema. Shortly, however, the characteristic changes are seen. They consist essentially of a combination of the following: an infiltration varying in density, limited rather sharply to the upper portions of the cutis and composed of a multiplicity of cell types, with pyknosis and karyorrhexis of the individual cells, and a tendency toward clumping of many of the cells. The cells comprising the infiltrate consist of eosinophils, polymorphonuclear leukocytes, connective tissue and cells of the vessel walls, as well as cells of

19. Warthin, A. S.: Lymphocytoma, in Osler, William: Modern Medicine, Philadelphia, Lea & Febiger, 1908, vol. 4, p. 827.

20. Mallory, F. B.: The Principles of Pathologic Histology: Lymphoblastoma, Philadelphia, W. B. Saunders Company, 1914, p. 325.

21. Cole, H. N.: The Cutaneous Manifestations of Hodgkin's Disease: Lymphogranulomatous, J. A. M. A. **69**:311 (Aug. 4) 1917.

22. Fox, Howard: Lymphogranulomatosis of the Skin in Hodgkin's Disease, Arch. Dermat. & Syph. **2**:578 (Nov.) 1920.

23. Fraser, J. F.: The Interpretation of Mycosis Fungoides as a Variety of Lymphosarcoma, Arch. Dermat. & Syph. **11**:425 (April) 1925; Mycosis Fungoides: Its Relation to Leukemia and Lymphosarcoma, ibid. **12**:814 (Dec.) 1925.

24. Keim, H. L.: Universal Leukemia Cutis, Arch. Dermat. & Syph. **10**:579 (Nov.) 1924; The Lymphoblastomas: Their Interrelationships, ibid. **19**:533 (April) 1929.

25. Ketron, L. W., and Gay, L. N.: Universal Lymphatic Leukemia of the Skin, Bull. Johns Hopkins Hosp. **34**:404 (Dec.) 1923.

26. Miller, H. E.: Lymphogranulomatosis Cutis (Hodgkin's Disease), Arch. Dermat. & Syph. **17**:156 (Feb.) 1928.

27. Symmers, Douglas: The Association of Certain Cutaneous Lesions with Diseases of the Hemopoietic System, J. Cutan. Dis. **37**:1 (Jan.) 1919.

28. Wile, U. J.: Cutaneous Manifestations of Systemic Disease, Ann. Int. Med. **5**:1103 (March) 1932.

29. Wise, Fred: Lymphadenosis Cutis Universalis, Associated with Generalized Erythrodermia and Atrophy of the Skin, J. Cutan. Dis. **35**:668 (Oct.) 1917.

the lymphocytic series. The formation of abscesses in the epidermis, simulating somewhat the condition seen in psoriasis, which has been emphasized as one of the diagnostic features of the disease, is of value but is not essential for diagnosis. The polymorphism of individual cells, in addition to the multiplicity of cell types and the clumping of endothelial cells, is the fundamental diagnostic criterion (fig. 4*a*). It is important, therefore, that the specimen taken for biopsy be carefully prepared, so as to avoid undue shrinkage of tissue, which may lead to an erroneous diagnosis. A definite diagnosis of mycosis fungoides often can be made on the basis of the criteria just named

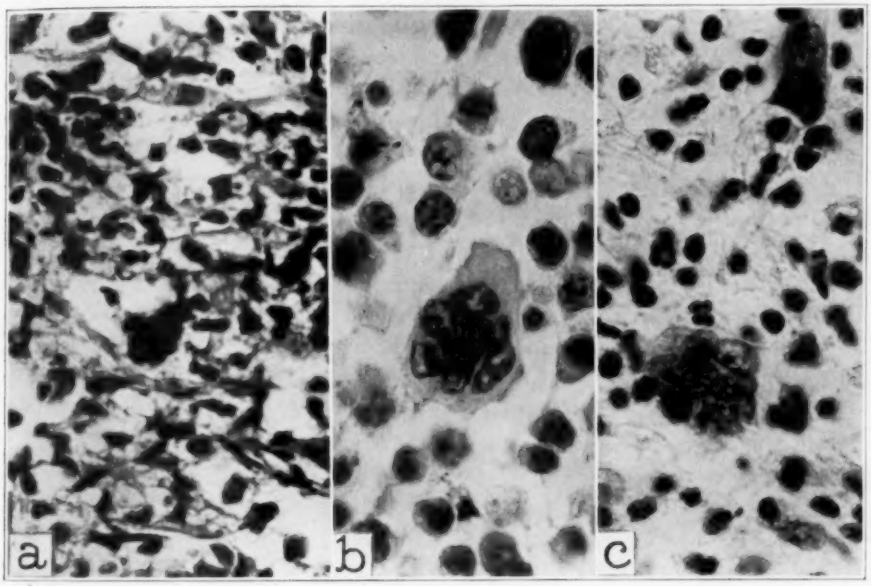


Fig. 4.—In *a*, mycosis fungoides: pyknosis of individual cells, multiplicity of cell types and clumping of cells (× 350); in *b*, Hodgkin's disease: typical Dorothy Reed cell (× 675); in *c*, dermatitis exfoliativa, lymphoblastoma of nonspecific type. The clumping of endothelial cells is to be distinguished from Dorothy Reed cells (× 675).

in the early stages of the disease, when the amount of infiltrate in the cutis may be even less than that usually seen in eczema or psoriasis. Mitotic figures are not prominent features until the stage of tumor is reached. In this later stage, the histopathologic picture may be far from specific, and it is regarding the appearance at this stage, too, that most of the controversy regarding the granulomatous or malignant nature of the disease arises. I have seen, in sections from one portion of a tumor, histopathologic changes typical of mycosis fungoides, and in sections from another part of the same tumor, a dense infiltrate of

lymphocytic cells, with numerous mitotic figures, thus presenting all the features of a lymphosarcoma.

It is my belief that mycosis fungoides is fundamentally a type of primary lymphoblastoma of the skin, which relatively infrequently involves the internal organs of the body in the same process. It can remain as mycosis fungoides throughout the course of the disease, or may at times eventuate in a lymphosarcoma, or in any other of the types of lymphoblastoma. Fraser's concept that the disease starts in the reticulo-endothelial system of the skin is worthy of careful consideration, but must be the subject of continued studies. An analogy can perhaps be drawn with Dörffel's [30] findings regarding the sarcoma of Kaposi. This condition, he showed, starts as an inflammatory reaction involving the reticulo-endothelial system of the skin; it may, however, eventuate in a truly malignant growth. I cannot agree with Symmers [31] regarding the abandonment of the term "mycosis fungoides," although I recognize that some cases which clinically fall in this classification may eventually prove, on microscopic examination, to be one of the other types of lymphoblastoma.

Any of the types of lymphoblastoma can start primarily in the skin, but, with the exception of mycosis fungoides, they usually present visceral manifestations of one sort or another when the cutaneous disease becomes manifest. True Hodgkin's disease of the skin is rare, and I do not believe that a diagnosis of Hodgkin's disease should be made without the demonstration of the typical Dorothy Reed [32] or Sternberg cell, the origin of which is still a subject of controversy. These singly nucleated, or multinucleated, giant cells are characterized by a deeply staining nuclear ring and a large, densely staining nucleolus; frequently, from four to ten nuclei are heaped together in the center of the cell (fig. 4*b*). Clumpings of endothelial cells (fig. 4*c*), which are frequently seen in cases of mycosis fungoides, but also in lymphoblastoma of nonspecific type, and occasionally in cases of benign dermatosis, are not to be confused with the true Dorothy Reed cells. These pseudogiant cells contain light-staining nuclei and small nucleoli. Just as in mycosis fungoides, so in Hodgkin's disease of the skin, there is a multiplicity of cell types in the infiltrate, but without polymorphism of the individual cells. Hodgkin's disease also may eventuate in lymphosarcoma. The infiltrate in both mycosis fungoides and in

30. Dörffel, Julius: Histogenesis of Multiple Idiopathic Hemorrhagic Sarcoma of Kaposi, Arch. Dermat. & Syph. **26**:608 (Oct.) 1932.

31. Symmers, Douglas: Mycosis Fungoides as a Clinical and Pathologic Nonexistent, Arch. Dermat. & Syph. **25**:1 (Jan.) 1932.

32. Reed, D. M.: On the Pathological Changes in Hodgkin's Disease, with Especial Reference to Its Relation to Tuberculosis, Johns Hopkins Hosp. Rep. **10**:133, 1902.

Hodgkin's disease extends up to the epidermis, causing secondary changes in the latter. Eosinophilia is not of any diagnostic significance, either in sections of tissue or in a differential blood count, for I have seen eosinophilia of 36 per cent in a case of eczematoid exfoliative dermatitis; in several other cases of benign dermatosis the number of eosinophils, both in smears and in sections of tissue, was greatly increased over that usually found in Hodgkin's disease.

Leukemia cutis is characterized by dense infiltration of the cutis with cells of the lymphocytic series or myelogenous leukemia by dense infiltration with cells of the myelocytic series. In lymphosarcoma, infiltration of the skin differs from that seen in lymphatic leukemia only in that numerous mitotic figures also are to be found. The infiltrate in both conditions presents a uniform character as compared with that of mycosis fungoides or of Hodgkin's disease. Although there is usually a border (*Grenz* zone) between the epidermis and cutis which is free from infiltrate, this is not always the case; the border is particularly likely to be absent, perhaps, in cases in which the disease has started primarily in the skin. The elastic tissue is destroyed where the infiltrate occurs.

Finally, there are cases in which the question is raised, on histopathologic study, whether the condition is a malignant epithelial neoplasm rather than a lymphoblastoma. The cases reported by Goeckerman and myself [33] and by Ketron and Goodman [34] are examples of this. I have seen two additional cases about which there has been a difference in opinion among pathologists. I still think, however, that these cases represent malignant invasion of the epidermis by cells of the lymphocytic series, rather than that the cells of the infiltrate are altered epithelial cells.

Eighteen of the ninety-five cases of lymphoblastoma presented universal exfoliation, and sixteen additional cases of the ninety-five presented generalized to universal erythroderma (table 2). The histopathologic picture in these groups differs in certain details, but not fundamentally, from that just given for the localized types of the diseases in question. A variable amount of involvement of the epidermis is seen, resulting either in acanthosis or in atrophy. As the result of eczematoid changes, or as the result of treatment, there may be a multiplicity of cell types in the infiltrate, which may make a diagnosis of leukemia or lymphosarcoma difficult. This accounts in part for the

33. Goeckerman, W. H., and Montgomery, Hamilton: Cutaneous Lymphoblastoma: Report of Two Unusual Cases, Arch. Dermat. & Syph. **24**:383 (Sept.) 1931.

34. Ketron, L. W., and Goodman, M. H.: Multiple Lesions of the Skin Apparently of Epithelial Origin Resembling Clinically Mycosis Fungoides, Arch. Dermat. & Syph. **24**:758 (Nov.) 1931.

fact that in more than half of the cases shown in table 2 a histopathologic diagnosis of a specific type of lymphoblastomatous involvement could not be made. These cases presented a dense infiltrate, usually limited rather sharply to the upper part of the cutis, although often extending down around the hair follicles and dermal glands. The infiltrate varied in character, usually reminding one of several of the types of lymphoblastoma at the same time, without being diagnostic of any one of them. Destruction of elastic tissue was seen where the infiltrate was present. The infiltrate was much more marked than that which is seen in an eczematoid or benign inflammatory exfoliative process. Also, the cutaneous pathologic changes were too marked to warrant classification of these cases as nonspecific reactions, namely, as so-called leukemids. It seems more likely that some of these cases represent primary involvement of the skin which has not as yet developed any specificity as to type. It is in this group particularly that it is necessary to employ all the additional diagnostic measures possible, including biopsy of a lymph node. In two cases in which a pathologic diagnosis of nonspecific type of lymphoblastoma was made, the cutaneous lesions have undergone complete involution. Wile, however, has recently pointed out that the cutaneous manifestations may undergo involution, and the patients remain apparently well for as long as four years, only finally to succumb to the disease. I made erroneous histopathologic diagnoses of lymphoblastoma in two cases before I realized that clumping of the endothelial cells (fig. 4*c*) in itself was not diagnostic of lymphoblastoma. The following cases of exfoliative dermatosis and malignant erythroderma are briefly cited to illustrate that the various problems in this group are the same as those of lymphoblastoma as a whole.

A patient presented marked exfoliative dermatitis (fig. 5), with associated generalized adenopathy. Studies of the blood, including a differential count, were reported as giving essentially normal results. The histopathologic changes in the skin were typical of mycosis fungoides.

In another case there was a similar picture of universal exfoliative dermatitis, with marked dystrophic changes in the nails. The histopathologic changes in the skin were consistent with the diagnosis of mycosis fungoides, except that there was little evidence of polymorphism of the individual cells; nevertheless, there was a multiplicity of cell types, and a clumping of endothelial cells was present (fig. 4*c*). On biopsy of a lymph node, the changes were reported as inflammatory. There were 19,600 leukocytes in each cubic millimeter of blood. The proportion of lymphocytes was 31 per cent, and mild secondary anemia was present. The blood picture, however, was not regarded as diag-

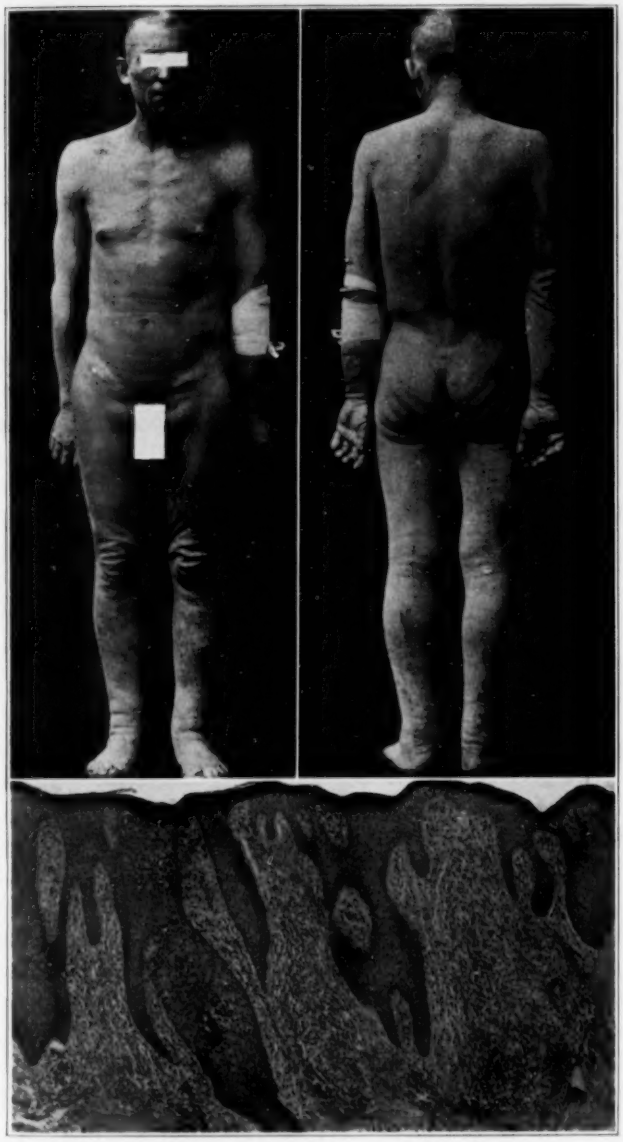


Fig. 5.—Dermatitis exfoliativa. Mycosis fungoides. Typical histologic picture: dense infiltrate limited to upper part of cutis and clumping of cells; also, early formation of abscess in epidermis (× 50).

nostic by the internist or by the hemocytologist. The infiltrate in the cutaneous sections was too marked to permit of classification of the case on the basis of benign or inflammatory change. The patient has been shown at several dermatologic meetings, at which the diagnosis of lymphoblastoma was concurred in.

Of still greater interest is a case of exfoliative dermatitis, in which the diagnosis originally made by the clinician and hemocytologist was infectious mononucleosis; later, the diagnosis was lymphatic leukemia; at postmortem examination the case presented all the features of Hodgkin's disease. When biopsy of the skin was made in the early stages of the disease, I reported: "The microscopic picture is consistent with the diagnosis of exfoliative dermatitis. It is not psoriasis. I cannot rule out early malignant erythroderma." When the sections were reviewed and further sections were cut, it was clear that the infiltrate was more marked than that seen in the benign types of exfoliative dermatitis (fig. 6), and in a few sections atypical Sternberg cells could be found. There were numerous eosinophils, but the predominating cell of the infiltrate was of the lymphocytic series.

In another case there was universal erythroderma (fig. 7), but without appreciable exfoliation. I made a diagnosis of leukemia cutis (lymphatic) on the basis of the cutaneous biopsy. On biopsy of a lymph node, the diagnosis made by surgical pathologists was lymphosarcoma. Leukocytes numbered 20,000 in each cubic millimeter of blood; yet the hemocytologists were unable to make a definite diagnosis of leukemia on the basis of the blood smear. A few months later the blood picture was typical of leukemia cutis, lymphatic in type.

In another case of exfoliative dermatitis, the clinical diagnosis was that of eczema. The histopathologic changes in the skin revealed a rather sparse infiltrate which, however, possessed most of the features of mycosis fungoides, so that I favored a diagnosis of lymphoblastoma. A little more than a year later, Barney [35] reported that the patient had typical discrete lesions of mycosis fungoides, and this was confirmed by a study of the histopathologic changes in the skin. On biopsy of a lymph node, the changes were reported to be inflammatory.

Although it will make the situation more complex, I wish to call attention to a case in which exfoliative dermatitis developed and was attributed to leukemia cutis on the basis of a count of 20,000 leukocytes in each cubic millimeter of blood, of which 60 per cent were lymphocytes. Shortly afterward, the patient was seen at the Mayo Clinic, at which time biopsy of a lymph node and blood smears revealed the picture typical of Hodgkin's disease. The cutaneous manifestations underwent complete involution, and the skin remained free from

35. Barney, R. E.: Personal communication to the author.

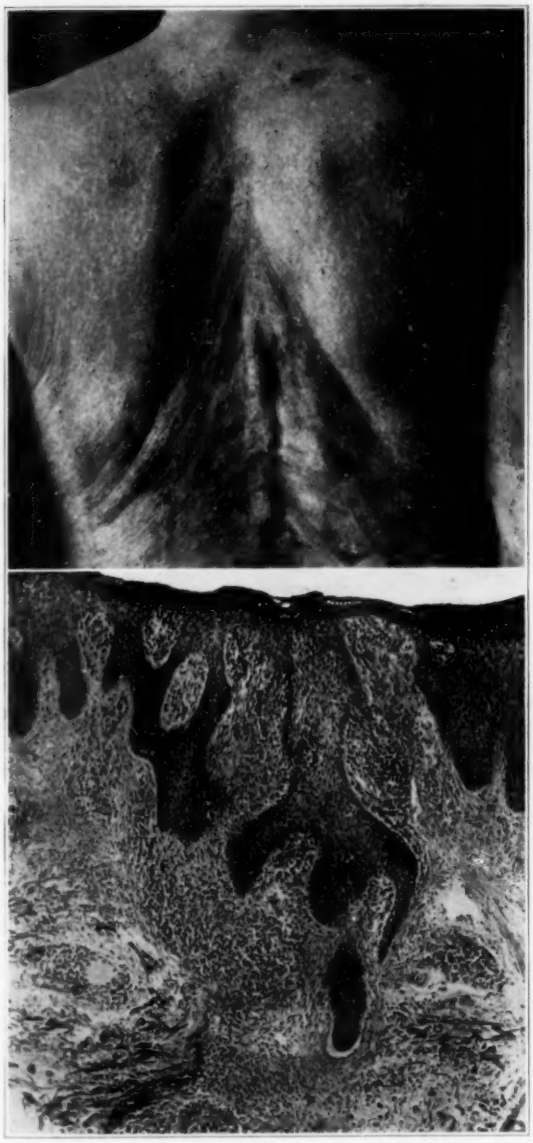


Fig. 6.—Dermatitis exfoliativa. Hodgkin's disease. Dense infiltrate composed of multiple types of cells, and giant cells which, with higher magnification, presented features of Dorothy Reed cells (× 75).

Fig. 7.—Universal malignant erythroderma. Leukemia cutis lymphatica. Dense infiltrate, chiefly perivascular, composed of cells of the lymphocyte series (× 80).

lesions for about two years. Numerous discrete plaques then developed, which on reexamination presented many of the clinical features of mycosis fungoides. Blood smears were no longer typical for Hodgkin's disease, but on several occasions biopsy of the skin was diagnostic of this disease. The diagnosis of Hodgkin's disease was confirmed at postmortem examination.

CONCLUSIONS

1. The histopathologic picture in erythroderma psoriaticum is diagnostic, or at least suggestive, of psoriasis in most cases, provided a suitable site for biopsy is chosen.

2. Exfoliative dermatitis secondary to other benign conditions can usually be distinguished from psoriasis on the one hand, and from lymphoblastoma on the other.

3. About 25 per cent of cases of exfoliative dermatitis proved, on microscopic examination, to belong in the group of lymphoblastomas.

4. The type of etiologic factors concerned in exfoliative dermatitis cannot be diagnosed on the basis of objective examination only. It is often necessary to use all the means at one's disposal, including biopsy of the skin and lymph nodes, the roentgen rays, studies of the blood and prolonged periods of observation, in order to arrive at the correct diagnosis.

5. Mycosis fungoides may start as exfoliative dermatitis, only later to assume its more common clinical appearance.

6. In several cases of exfoliation or universal malignant erythroderma, primary specific changes of one of the types of lymphoblastoma were found in the skin before such changes were seen either at biopsy of a lymph node or in the course of studies of the blood.

7. The histopathologic report that an excised lymph node presents merely an inflammatory reaction does not rule out the possibility that the exfoliative dermatitis may be of lymphoblastomatous etiology.

8. Although the cutaneous histopathologic picture in exfoliative dermatitis and malignant erythroderma may present the features of lymphoblastoma, in more than half of the cases it is impossible definitely to specify which type of lymphoblastoma will eventually develop.

9. The interrelationship of the various types of lymphoblastoma is considered. In a few cases the cutaneous manifestations cleared, only to return in another form after a variable period of remission.

ABSTRACT OF DISCUSSION

DR. WALTER J. HIGHMAN, New York: The findings in this paper are precisely what any one who has the pleasure of knowing Dr. Montgomery well would have expected. It was particularly delightful to me to have him read this paper, as I plan to devote some time to this study myself and am glad that the details will not have to be allotted to me.

It was particularly interesting that Dr. Montgomery pointed out so clearly the fact that the concept of erythroderma is a concept of an extrinsic and not of an intrinsic disease. Erythroderma reveals itself only on minute study, and it maintains the same character under the microscope. That which arises in psoriasis remains psoriasis. The truth of this is of particular significance in the histologic interpretation of all the findings in the erythrodermic stage in dealing with these diseases. Work as clear as that of Dr. Montgomery acquires a practical as well as a scientific aspect. In all this group we can be sure that the conditions clinically designated are clinically definite. This statement has nothing to do with etiologic concepts. It remains true that what we are pleased to call leukemia, lymphosarcomatosis and so on are histologically entirely different from mycosis fungoides. The last does not microscopically look like the others, and we can, therefore, use it as a scrap heap called mycosis fungoides. Personally, I do not subscribe to this belief, nor to the belief that all are intimately related. Dr. Fraser is pleased to call the essential mycosis cell mesenchymal, and Klemperer calls it the embryonal cell. The point is that there must be an embryonal cell from which these conditions arise, and this must explain, until we have better proof, the fact that we have various types, as indicated in one case, and as brought out in Dr. Lane's case. With these considerations in mind, and not wishing to monopolize more time, and in order to leave something for Dr. McCarthy, who is also a histopathologist like me (God save the mark), to say nothing of Dr. Weidman, I shall stop.

Dr. C. L. McCarthy, Washington, D. C.: Dr. Highman has already said all the nice things I wished to say in congratulating Dr. Montgomery on his excellent paper. However, I wish to ask Dr. Montgomery whether he has included pityriasis rubra pilaris in this group of cases. Of course, it is well known that we must distinguish two types of this disease, one in which there occurs only a papular eruption, and a second type in which there exists a generalized exfoliating dermatitis. Separation of this type of the eruption from the disease mentioned by Dr. Montgomery is not always possible by histologic examination. Therefore, I think that any general consideration of diseases of exfoliating dermatitis should include the exfoliating type of pityriasis rubra pilaris.

Dr. Samuel Sweitzer, Minneapolis: I wish to emphasize the necessity of determining the causal factor in these cases. Recently we have had two cases in the hospital, one due to psoriasis and the other due to arsenic in a patient with ichthyosiform erythroderma. We have tried Dr. Goeckerman's treatment for exfoliative erythroderma in psoriatics and found that it gives excellent results. It is particularly important to do a biopsy in these cases, and if we find them psoriatic we should use the lamp and tar treatment of Dr. Goeckerman.

Dr. William Allen Pusey, Chicago: Dr. Montgomery's paper illustrates well something not entirely pertinent to the topic, and that is the summarization of papers. Dr. Montgomery gives a good illustration of what the summary of conclusions should be. We are constantly having to waste space on so-called summaries that are not worth the space they take up. My attention was called to this by one of the best medical men in the country, who is also an editor. I hope you will give us less illustrations that are not important, and remember that the main point in summarizing a paper is to abstract the points that are being made. I returned a paper to one of our colleagues with this suggestion, with a copy of this man's letter, and he brought back a very good point, that it would be a good plan in writing a paper to make an abstract and then one would have the author's idea of what constituted the paper. Dr. Montgomery's summary is so good that it offers an excellent text for these remarks.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: I wish to thank the discussors for what they have said. In regard to pityriasis rubra pilaris, I think it should be sharply differentiated from lichen ruber planus. I have seen quite extensive exfoliation in pityriasis rubra pilaris, but none of the cases from which a biopsy specimen was taken was extensive enough to warrant the designation exfoliative dermatitis. (Since then I saw one case of exfoliative dermatitis due to pityriasis rubra pilaris in which the biopsy presented all the features of the disease in its localized form.) In the histopathologic data that I have given in my paper, I have purposely avoided discussion regarding etiology. Thus, for instance, the pathologists are not in entire agreement as to the origin of the Dorothy Reed cell of Hodgkin's disease. I have merely tried to give the outstanding characteristic or diagnostic features of the disease in question and to show that with careful histologic study together with correlation of the other clinical and laboratory procedures it is possible to distinguish between exfoliative dermatoses of the benign type on the one hand and of lymphoblastomatous etiology on the other.

TRICHOSTASIS SPINULOSA

S. J. FANBURG, M.D.
Assistant Attending Dermatologist New York University and Bellevue Hospital Medical College
NEWARK, N. J.

A review of the twenty-one cases of trichostasis spinulosa recorded in the literature gives one the impression that the disorder is rare and occurs only in men beyond the age of 30. Williams, in the discussion of the paper by Burgess,[1] stated that he thought the condition was common in persons over 50. That trichostasis spinulosa is by no means a rarity would seem to be indicated by the fact that I have been able to observe twelve cases in the course of two months. No cases in women or children have previously been reported. Two of my cases were in women and one in a boy 6 years of age.

REPORT OF CASES

CASE 1.—R. L., a woman, aged 21, came to the skin clinic of New York University and Bellevue Hospital on account of scarring following furuncles of the face. Examination of the skin revealed numerous blackish dots scattered over the front and sides of the nose. A faint scaliness was visible. The skin was not oily. On palpation, the nose felt rough, as if covered with tiny spines. The contents were expressed from several of the follicles and under the low power lens of the microscope were found to contain the typical "Pinselhaar." There were from ten to thirty hairs in each bundle. Some of the bundles were enclosed in horny sheaths, and others were naked. The patient thought that the condition on her nose had been present for about two years. No other areas were involved.

CASE 2.—L. L., a girl, aged 19, a sister of the patient in case 1, was being treated at the clinic for seborrheic dermatitis of the scalp. Examination revealed trichostasis spinulosa of the nose, interspersed with ordinary comedones.

CASE 3.—S. R., an Italian boy, aged 6, came to the clinic to be treated for tinea capitis. Over both cheeks, extending from the malar regions laterally, were numerous tiny black dots which felt rough to the touch. Microscopic examination of the follicular contents in these areas showed the typical hairs of trichostasis.

CASE 4.—E. F., a man, aged 33, presented himself at the clinic on account of furunculosis of the neck. Examination showed that he had also trichostasis spinulosa of the nose. The patient stated that he had had what he thought were "blackheads" for about ten years.

CASE 5.—S. F., a man, aged 29, had noticed a slight roughness of the forehead for about a year. On close examination, brownish-black plugs could be seen pro-

Submitted for publication, July 2, 1932.
From the Department of Dermatology and Syphilology, New York University and Bellevue Hospital Medical College, service of Dr. Howard Fox.

1. Burgess, J. F.: Trichostasis Spinulosa, Arch. Dermat. & Syph. **25**:40 (Jan.) 1932.

jecting from the follicles in the midline of the forehead, extending laterally about 2 cm. to the hairline. Microscopic examination of the expressed follicular contents revealed the typical bundles of hair.

CASE 6.—H. D., a man, aged 27, consulted me on account of the "blackheads" on his nose of ten years' duration. Over the front and sides of the nose were tiny black follicular dots. The skin was not oily, and there were no other lesions. Examination showed that each follicle contained the typical hairs of trichostasis.

CASE 7.—B. A., a man, aged 30, was not conscious of any disturbance of his skin. Examination showed trichostasis spinulosa limited to the nose.

CASE 8.—H. S., a man, aged 39, thought that he had had "blackheads" on the nose for about twenty years. Numerous black follicular plugs, which were slightly

Trichostasis spinulosa of ten years' duration on the nose of a man aged 27 (case 6).

rough to the touch, were present all over the nose. The affected skin was dry. Microscopic examination revealed trichostasis spinulosa.

CASE 9.—A. A., a man, aged 41, came to the clinic to be treated for psoriasis. He had also, on the anterior tip of the nose, five or six black follicular puncta. Trichostasis spinulosa was found on microscopic examination of these follicles.

CASE 10.—S. M., a man, aged 39, had black follicular plugs on his nose, which resembled comedones, but which on microscopic examination proved to be typical "Pinselhaar."

CASE 11.—S. S., a man, aged 29, had had what he thought were "blackheads" on his nose for about ten years. Microscopic examination of the follicular plugs revealed trichostasis spinulosa.

CASE 12.—J. E., a man, aged 27, had numerous brownish-black follicular plugs on his nose, which on examination were seen to consist of the typical hair bundles.

COMMENT

The literature on trichostasis spinulosa was reviewed by Mitchell [2] in 1925. Since then Maloney [3] and Burgess [1] have each reported one case. Burgess described the histologic picture, and came to the conclusion that in trichostasis spinulosa "numerous resting buds exist in the same follicle, and that these, in response to an unknown stimulus, develop the numerous individual hairs of immature type, and that this stimulus at the same time gives rise to an associated hyperkeratosis that even extends down to the origin of the hair." The fact that trichostasis spinulosa has been thought so rare may be ascribed to faulty observation, in my opinion. It is not even necessary to use a microscope in making the diagnosis. If, after expression, the contents of a follicle are placed on a piece of white paper or a glass slide, and then teased apart, the individual hairs may be easily discerned with an ordinary magnifying glass.

SUMMARY

1. Two previously unrecorded cases of trichostasis spinulosa in women and one case in a boy are here reported.

2. Twelve cases of trichostasis spinulosa collected in two months would seem to indicate that the condition is not rare.

NOTE.—Since this paper was submitted for publication about fifty additional cases of trichostasis spinulosa have been observed in adults; most of these were limited to the nose.

31 Lincoln Park.

---

2. Mitchell, J. H.: Trichostasis Spinulosa or Pinselhaar, Arch. Dermat. & Syph. **11**:80 (Jan.) 1925.

3. Maloney, E. R.: Trichostasis Spinulosa, Arch. Dermat. & Syph. **24**:1135 (Dec.) 1931.

BASAL CELL EPITHELIOMAS WITH EXCESSIVE PIGMENT FORMATION

THEIR RELATION TO MELANOMAS

JOSEPH JORDAN ELLER, M.D.
NEW YORK
AND
NELSON P. ANDERSON, M.D.
LOS ANGELES

Basal cell epithelioma is undoubtedly the most common variety of cancer involving the skin. But in spite of its well known clinical and histologic appearances, there is but little information in the literature concerning the type which is associated with pigment. It is true that a few cases in which pigmentation was a marked, if not a predominating, feature have been presented before dermatologic societies in this country and in Cuba. However, these cases have occasioned little comment from dermatologists.

Without histologic examination, an excessively pigmented basal cell epithelioma may easily be confused with melanoma. In view of the preoperative diagnosis of melanoma in our first case, it is not unlikely that in the past a considerable number of similar "melanomas" have been mistakenly diagnosed, treated and cured. For this reason we believe that the following cases, which are by no means unique and yet are comparatively rare, are worthy of report.

REPORT OF CASES

CASE 1.—F. W., a man, aged 34, of dark complexion, was first seen on March 13, 1929 (in consultation with Dr. J. Frank Fraser, who permitted us to present this case). The patient had a lesion involving the lateral portion of the right lower eyelid. According to the history, it had been present since birth (the patient stated "as long as he could remember"). For the past three months he had been aware of considerable irritation in the lesion, and recently, on washing his face, he had noted that bleeding readily occurred.

On examination (fig. 1), the lesion involving the lateral portion of the right lower eyelid measured approximately 2 by 2.5 cm. With the exception of one or two small split pea-sized nodules, the lesion was not elevated, but on the contrary seemed level or slightly depressed. No induration was present. Scattered throughout the involved area, which was yellowish brown, were from eight to ten small pinhead to split pea-sized bluish-black areas. The palpebral conjunctiva was not involved. The regional lymph nodes were not palpable.

It was the opinion of Dr. Fraser and ourselves that the lesion was a peculiar type of nevus which was undergoing or had undergone malignant change (melanoma). Therefore, an unfavorable prognosis was given, and the lesion was excised widely by means of the endotherm knife.

Histologic examination revealed an unusual picture (fig. 2). Microscopically, the section was that of a typical basal cell epithelioma. In the cutis, however, sometimes superficial and sometimes deep, were large masses and clumps of pigment. Nowhere were nevus cells or those suggesting the structure of a nevus found.

These sections were studied by Dr. James Ewing, who concurred with Dr. Fraser's previously expressed opinion, that the lesion was a typical basal cell epithelioma with an unusually large amount of pigment. Since that time other sections from the same lesion have been studied by Drs. Wile, Weidman, Finnerud, Morrow, McCarthy, Highman, Michelson, H. Montgomery, Way, Becker, Satenstien, P. Masson, Pautrier and Bruno Bloch. With the exception of Pautrier, they have all agreed with the histologic diagnosis as given.

Fig. 1 (case 1).—Lesion near the lateral margin of the lower eyelid. The patient had had the mark as long as he could remember, but it had begun to bleed recently. The clinical diagnosis was nevus with melanotic degeneration, but histologic examination of the excised specimen revealed typical basal cell epithelioma with an unusually large amount of pigment. See figure 2.

Silver nitrate impregnations revealed most of the pigment to be in the chromatophores in the cutis and in the dendritic cells in the tumor. A small amount of fine pigment was found in the tumor cells.

Case 2.—L. V., a Mexican laborer, aged 50, was first seen by one of us on March 20, 1931. At that time he presented a small hazelnut-sized tumor on the left side of the chin. It was difficult to obtain a satisfactory history, but he stated that for many years he had had a dark mole in this area. About eight years previously, the mole had been injured while he was shaving. Thereafter, the lesion began to grow and gradually increased in size to its present state. Two

months before he was first seen, the lesion had again been injured while shaving, and since then had occasionally bled on provocation.

Examination revealed a small hazelnut-sized growth on the left side of the chin, which measured 1.5 cm. in diameter and presented a small area of ulceration in the nodule. The entire tumor was from bluish black to black. There was distinct evidence, however, of that peculiar translucence which one clinically associates with typical basal cell tumors of the skin.

In view of these findings and our experience in the previous case, a provisional diagnosis of basal cell epithelioma associated with pigmentation was made.

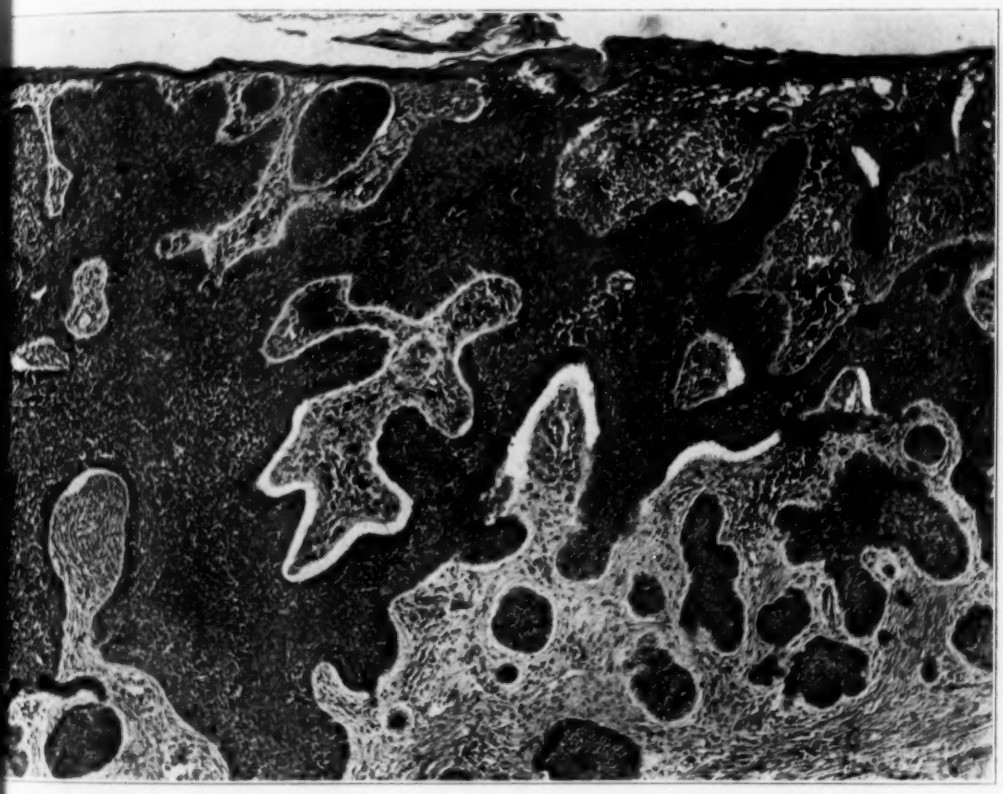


Fig. 2 (case 1).—Microscopic section through the specimen. The picture is typical of basal cell epithelioma. Note the large masses and clumps of pigment in the cutis.

Nevertheless, melanoma could not be entirely ruled out clinically. The lesion was widely excised by the endotherm knife and the tissue examined histologically.

The histologic findings were similar to those in case 1. The report on the tissue by Dr. E. M. Butt was as follows:

"Specimen is that of a small piece of skin containing a tumor mass which presents some tiny areas of pigmentation. Diameter of tumor 1.5 cm. Sections show numerous large bulky well circumscribed masses of somewhat fusiform

epithelial cells deep in the corium. In some of the masses a few of the cells are filled with a golden brown and a brownish black pigment. There is an occasional mitotic figure. The fibrous tissue stroma between the masses of cells is heavily infiltrated with leukocytes.

"Diagnosis: Carcinoma, basal celled, pigmented."

The tumor had undoubtedly arisen from the sheaths of the hair follicles and, while some of the tumor cells contained a small amount of pigment, the majority of the pigment seemed to be contained within the chromatophores. The degree of pigmentation was less marked, as a whole, than in case 1.

REVIEW OF THE LITERATURE

Study of the literature proves that such cases are not common. While Bloch [1] (in his article on pigment in Jadassohn's "Handbuch der Haut- und Geschlechtskrankheiten") mentioned the fact that occasionally the basal cells in basal cell epithelioma produce an increased amount of pigment, yet in these cases the pigment is definitely related to the basal cells and practically remains within them.

Pardo-Castello [2] presented a case of "pigmented basal cell epithelioma" before the Cuban Dermatological Society on Oct. 4, 1928, and in a personal communication stated that he had observed three other cases. In the discussion which followed, he pointed out that, from their appearance, such lesions are apt to be diagnosed as melanomas. However, his histologic section plainly showed the pigment to be intracellular and mostly confined to those basal cells which formed the border of the neoplastic cell masses.

Through the courtesy of Dr. Pardo-Castello, we are reproducing one photograph representing a case of basal cell epithelioma with excessive pigment formation (fig. 3).

Chambers and Stokes,[3] on Dec. 3, 1926, presented before the Philadelphia Dermatological Society a pigmented basal cell epithelioma in which there were unusually large pigmented cells in the basal layers and in a few of the extensions below that level.

Nomland [4] showed an interesting case of multiple superficial epitheliomas. In his case one of the lesions presented areas containing many pigment-bearing cells and also free pigment. From the histologic description, this one lesion was a basal cell epithelioma with pigment.

---

1. Bloch, Bruno: Pigment, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1927, p. 531.

2. Pardo-Castello: Pigmented Epithelioma, Arch. Dermat. & Syph. **19**:691 (April) 1929.

3. Chambers and Stokes: Basal Cell Epithelioma, Arch. Dermat. & Syph. **15**:722 (June) 1927.

4. Nomland: Epitheliomatosis: Multiple, Superficial, Arch. Dermat. & Syph. **20**:754 (Nov.) 1929.

Gross [5] exhibited before the New York Academy of Medicine an interesting case in which a woman presented an elevated, somewhat verrucous, deeply pigmented tumor in the left infrascapular region. This lesion had been present for fifteen years. In the discussion, melanoma and Bowen's disease were mentioned as additional diagnostic possibilities. The lesion was removed by wide surgical excision. Histologic study of the excised tissue showed a typical basal cell epithelioma with considerable pigmentation.

O'Donovan,[6] among thirteen cases of carcinoma of the hands occurring in women, mentioned one case in a patient, aged 56, who had a melanotic basal cell carcinoma of the skin of the wrist. Further personal communication with Dr. O'Donovan, and through him with Prof. Hubert M. Turnball of the Bernhard Baron Institute of Pathology

Fig. 3.—Basal cell epithelioma with excessive pigment formation at the outer canthus of the eye (courtesy of Dr. Pardo-Castello).

of the London Hospital, revealed that in his case "the growth is only a common form of malignant melanoma or melanotic carcinoma of the skin. It is not a basal cell carcinoma of ordinary nomenclature with melanotic pigmentation."

Montgomery,[7] in his work on superficial epitheliomas, called attention to the occurrence of pigment in basal cell cancers, remarking that "in several cases, as shown by staining with silver nitrate, a varying amount of melanin pigment was found in the basal cells of the epidermis,

5. Gross: A presentation of a case before Sect. Dermat. & Syph., New York Acad. Med., December, 1929.

6. O'Donovan, W. J.: Cancer of the Skin Due to Occupation: Tar Carcinoma, Arch. Dermat. & Syph. **19**:595 (April) 1929.

7. Montgomery, H.: Superficial Epitheliomatosis, Arch. Dermat. & Syph. **20**: 339 (Sept.) 1929.

in dendritic cells about the tumor and rarely in the tumor cells. In addition, there was a varying number of chromatophores laden with pigment limited to the papillary bodies."

Bloch [8] has recently reported four interesting cases, which will be discussed later.

Schröpl [9] also commented on the infrequency of pigmented basal cell epithelioma and added two cases. He believed that his cases corresponded in histologic structure with the first of four cases of non-nevoid melano-epitheliomas of the skin described by Bloch (see under "Origin of Cutaneous Pigment).

Under the title of lentigo maligna, Shaw,[10] in 1931, reported a case closely related to the group under consideration. It occurred in a white woman, aged 79, and was characterized by a slowly progressing, pigmented lesion of long duration, giving rise to seven pigmented epitheliomas during six years of observation. The interesting features in this case were the prompt response of the epitheliomas to radium therapy, the complete depigmentation of the irradiated areas, apparently temporary, since the pigment tended to reappear at the periphery of the area and spread slowly inward, and the absence of a recurrence, even after six years in the case of the first epithelioma treated.

From histologic examination, Shaw said: "This tumor is no doubt malignant and is most probably of the basal-cell type with a squamous-cell anaplasia. In other words, it is a tumor of low-grade malignancy." The growth contained mitotic figures and occasionally an attempt at pearl formation. In the subepithelial layer, the pigment was finely granular. Deep in the corium, and especially surrounding the glandular elements of the skin, it was clumped into masses.

The reported or presented cases of basal cell epitheliomas with pigment appear, then, to be quite uncommon. This may be because they are actually rare, which is probably the case, or because of the unfortunate fact that many, if not most, basal cell epitheliomas and melanomas are diagnosed and treated without any histologic confirmation.

ORIGIN OF CUTANEOUS PIGMENT

The origin and nature of cutaneous pigments, particularly melanin, constitute one of the most interesting fields in dermatology. The excellent and painstaking researches of Bloch and the contributions of

8. Bloch, B.: Ueber benigne, nicht nævoide Melanoepithelioma der Haut nebst Bemerkungen über das Wesen und die Genese der Dendritenzellen, Arch. f. Dermat. u. Syph. **153**:20, 1927.

9. Schröpl, E.: Ulcus rodens pigmentosum, Arch. f. Dermat. u. Syph. **154**: 61, 1927.

10. Shaw, H. C.: Lentigo Maligna: Report of One Case Treated with Radium, Am. J. Cancer **15**:1557, 1931.

Masson, Caudière, Miescher, Becker and others have been most instructive. According to Bloch:[11]

The ectodermal pigment of the skin and also of the mucous membrane is found in the epidermis (or epithelium) particularly in the basal cells, in the hair matrix and in the cells of the pigmented nevi which develop through a metaplastic process from the epidermal cells.

All these form the pigment that they contain in their protoplasm; they are therefore melanoblasts[12] of ectodermal origin.

The mesodermal part of the skin or corium contains two entirely different kinds of pigment cells.

One type is found regularly but in varying numbers in the papillae and also in the deeper layers. They are plump, sometimes somewhat branched cells of very variable form containing coarse granules of pigment. These are the chromatophores and they do not form the pigment themselves. They are connective tissue cells which have phagocytized pigment which was originally found in the epidermis.

HISTOLOGIC CONSIDERATIONS

The basal cells of the epidermis apparently possess two functions, the main one being that of reproduction. The basal cells have always been considered the germinative cells of the epidermis, e. g., those cells which give rise to the rest of the epidermal elements. A second function, that of the formation of pigment, is less understood but nevertheless exists, as shown by Bloch and others with reactions to dioxyphenylalanine.

As Way[13] stated, "if one accepts the theory that pigment is formed through a special activity of the cells of the germinal layer of the rete malpighii and also that carcinomas of the basal cell type rise from the epidermis or its accessory structures, it seems rather strange that pigment bearing epitheliomas of the basal cell type are not more frequently seen." He further remarked that he has rarely found pigment in the corium in true basal cell carcinoma. In only two of his collection of several hundred specimens of carcinoma did he find evidence of pigment (epidermal excepted). One of these sections was from a paraffin worker, and the occupation of the person from whom the other section was taken was not known. He did not state whether these two epitheliomas were of the basal or the prickle cell type. In one at least (paraffin worker) it was probably prickle cell in type.

---

11. Bloch, B.: Problem of Pigment Formation, Am. J. M. Sc. **177**:609, 1929.

12. "We call melanoblasts those cells which are capable of forming pigment, while those which contain pigment which they themselves have not elaborated but have only obtained elsewhere (absorbed or phagocytized) are called chromatophores or melanophores." Bloch[1] points out that it would be "helpful if genesis and pigment formation were disregarded and the pigment cell were commonly called melanocyte, the autochthonous pigment forming cell melanoblast, the phagocytic pigment cell melanophore, and the ambiguous term chromatophore were dropped."

McCarthy [13] expressed the belief that in the evolution of basal cell epitheliomas "the first function disturbed is that of pigment production" and, although admitting that he had no definite proof of this, considered that "the first change that takes place is an increased production of pigment. This is borne out somewhat by the fact that the limiting cells of the nests are always darker than the younger ones. This disturbance of the pigment function results in the production of large amounts of pigment which in most cases appears early in the connective tissue of the corium and papillary bodies."

In a more recent communication, Bloch,[8] in presenting four cases of "benign and non-nevoid melano-epitheliomas of the skin," stated that no similar cases have appeared in the literature.

In his first case, he noted histologically that the epithelial columns forming the tumor were perpendicular to the surface and were composed of three different types of cells: (1) basal cells, (2) cells of the spicular type, with centrally formed cornified pearls and containing little or no pigment and (3) pigmented cells of dendritic structure, which were irregularly interspersed with the cells of the first type (basal cells) and in many areas exceeded the basal cells in size as well as in number. These dendritic cells possessed many irregular processes containing numerous melanin granules and, while dispersed throughout the tumor, were found mostly in the basal parts. Aside from the dendritic cells, there were some cells with short, abortive processes and transitions of the cells of the basal type without dendrites. In the connective tissue stroma of the tumor, there were a marked degree of inflammation in certain areas and an enormous amount of pigment. The pigment was found in large globules, partly free, but mostly within connective tissue cells as well as in the endothelium and in the lumen of the dilated papillary vessels. Bloch considered this case as a mixed tumor, an epithelioma in the sense of Darier, the structure of which not only is basocellular and spinocellular, but also contains dendritic melanoblasts. Based on the histologic findings, he regarded the entire structure as benign and stated that the tumor might be called a "melanotic benign (pre-cancerous) skin epithelioma with three different cell types (basal, spinocellular dendritic)."

In Bloch's second case, there was a solitary papillary nodule with a dark blue-brown color clinically similar to an early nevocarcinoma that is progressing slowly. Histologically, it was an epithelial tumor originating from the epidermis and composed entirely of cells of the basocellular type. The corium was almost entirely free from pigment, and there were no dendritic melanoblasts. Pigment was found mostly in the basal-like tumor cells. This tumor Bloch designated as a "benign

13. Personal communication to the authors.

melanotic skin epithelioma of uniform baso-cellular type without dendritic cells and almost without chromatophore pigments."

The third case, Bloch believed, belonged to the same group as his second case, the only difference being that "there was no pure baso-cellular character, the chromatophore pigments being present in abundance."

The fourth case was identical with the second.

In commenting on the extraordinary differences of the relation of the pigment in the first two cases, Bloch remarked:

> In the first case the pigment predominated in the melanoblasts of dendritic structure, so that in many sections one would think of a melanoblastoma or dendronoma. In the cells of the pure basal type and in the spinocellular nests the pigment was much reduced in quantity. Only in a relatively few areas, the non-dendritic cells exhibited some pigmentation. As a rule they possessed only a few granules but no pigments. Of further significance was the accumulation of chromatophore pigments in the stroma.
>
> In contrast to the above we find in the second tumor in spite of the just as marked pigmentation, no dendritic cells. They are the non-dendritic basal-like tumor cells which contain the pigment in the protoplasm predominantly in the vicinity of the nuclei, never in the processes. Stroma pigments in this case are scarcely found.

An explanation of these findings, Bloch admitted, is quite difficult with the present knowledge of the metabolism of pigment.

> All authors agree that the dendritic cells form their own pigment and are therefore autochthonous melanoblasts. The origin of the dendrite cells and their relation to the non-dendritic cells is not fully explained. The simplest view is that the dendritic cells genetically belong to the common basal cells and represent a functionally highly differentiated morphologically specialized variation of the cell. . . . The relation of dendritic cells to the nervous skin elements, especially to those described by Langerhans, cannot be stated definitely. It may however be stated that the structure described by Langerhans with the dendritic melanoblasts has nothing to do with the pigment formation and therefore the expression "Langerhans cells" is not proper for these melanoblasts.

Caudière,[14] speaking of the occurrence of pigment in certain basal cell epitheliomas, concluded that in certain "epitheliomas malphigiens cutanes," either basocellular or spinocellular, one can see the neoplastic formations encroached on by pigmented ramifying cells, especially abundant in superficial regions. These cells are nothing else but Langerhans cells of the normal epidermis, which, on contact with neoplastic elements, can, under certain conditions, undergo hyperplasia and mobilize themselves. By a process of active migration, probably due to a certain ameboid power, they can insinuate themselves between can-

14. Caudière, M.: Recherches sur l'évolution des cellules pigmentaires dans certains épithéliomas envahissant l'épiderme, Ann. d'anat. path. **3**:119, 1926; Evolution of Pigmented Cells in Certain Malpighian Epitheliomas of Skin, Compt. rend. Soc. de biol. **94**:339, 1926; Ann. d'anat. path. **3**:134, 1926.

cerous cells and penetrate to a certain depth. Segregated in this way, the Langerhans cells keep, for a certain time at least, their pigment-forming function and do this following a process comparable to the normal process elaboration of the dioxyphenylalanine-oxydase and of true pigment.

According to Caudière, only a comparative study of these elements by the reaction to dioxyphenylalanine and by silver impregnation permits one to determine exactly in any particular instance the histophysiologic state of these elements. The finding of cells presenting a positive reaction to dioxyphenylalanine and some positive impregnation of silver and having, then, the characteristics of a melanoblast with preserved elaborative activity, or cells containing some grains of acquired silver reduction pigment but having a negative reaction to dioxyphenylalanine, permits the conclusion of the absence of actual elaboration of oxydase and of pigment.

As in tumors of the breast, Caudière considers that the melanoblasts determine the pigmentary surcharge of the macrophages contained in the connective tissue of the neighborhood. In an accessory way, they seem to be able to pigment the neoplastic cells among which they live; but in "epitheliomas malphigiens" the last condition seems rare and of small importance, at least in the cases Caudière has observed. In every case the pigment leaves the melanoblasts only in a state of true finished pigment. Caudière never observed granules (dioxyphenylalanine positive) in any place other than the melanoblasts.

Caudière cautioned against insisting too much that tumors of the type under consideration have nothing in common with the nevo-epithelioma. They are in a way different in all their characteristics. They are only "epitheliomas malphigiens spinocellular or baso-cellular" encroached on by the cells of Langerhans, which live in symbiosis with their elements. Caudière considered them "epitheliomas malphigiens" with symbiotic pigmentary cells. "They are not tumors pigmenting; they are tumors pigmented."

According to the views of Masson and Caudière, based on the assumption of a neurogenic derivation, the melanoblasts and the cells of Langerhans are essentially equivalent and should be distinguished from the epithelial cells. This view is not in accord with Bloch's ideas.

COMMENT ON AUTHORS' CASES

The interesting or rather unique feature of the histology in our first case is the fact that the pigment was contained chiefly in the chromatophores and was practically limited to the corium, although slides stained [15] with silver nitrate and counterstained with hematoxylin

15. Courtesy of H. Montgomery, the Mayo Clinic.

revealed, in addition, pigment in dendritic cells both in the basal cells of the epidermis and in the tumor.

One would believe with Way that, since the basal cells are concerned with the formation of pigment, there should be a considerable number of basal cell carcinomas with an increased amount of pigment. This does occur, but is infrequent in our experience. Montgomery,[14] however, does not believe that basal cell epitheliomas with pigment are rare, and he mentioned seeing, "with Broders, quite a number of ordinary basal cell epitheliomas which contained varying amounts of pigment, even to the point of the tumor cells containing a great deal of pigment." He also mentioned the great amount of pigment seen in seborrheic keratoses, in dermatosis papulosa nigra (of Castellani and Michael) and in the early epitheliomatous lesions of xeroderma pigmentosum.

Masson,[13] after studying the slides in case 1, expressed the opinion that "its pigmentation is due to a very peculiar property of the epidermic melanoblasts. These migrate into the epithelial tumors which invade the epidermis to a certain depth and eliminate pigment that is phagocytized by the histiocytes of the stroma." He expressed the belief that this phenomenon is similar to that occurring in cancers of the breast invading the epidermis.

Bloch,[13] after staining the preparations from case 1 with silver nitrate and various dyes, arrived at the diagnosis of a richly pigmented basal cell carcinoma with loss of the epidermal pigment produced by the melanoblasts of the epidermis (so-called *incontinentia pigmenti*). He observed many typical dendritic cells (melanoblasts) among the basal cells of the epidermis and of the tumor cells themselves, which contained small pigment granules. With the silver reaction, this was well observed. According to Bloch, the pigment granules of epidermal origin dropped into the corium and were there phagocytosed by cells of mesodermal origin, which by this process became chromatophores. The chromatophores contained more pigment of a darker color, and were therefore more visible and impressive than the melanoblasts of the epidermis and the tumor. To them Bloch attributed the dark bluish color of the whole tumor. Histologically, he found no sure traces of a nevus. In some spots in the epidermis Bloch saw cells which were not connected normally with the surrounding cells and which bore a little resemblance to a beginning nevus, but he had the impression that these were artificial products caused by traumatism and fixation.

Weidman, after studying the sections in case 1, remarked "that the presence of so many hair follicles within the cancerous masses is one of the most interesting points of the section and points clearly to its origin from the sheaths of the hair follicles." He observed several mites (Demodex folliculorum) in one of the dilated follicles. Commenting on the "occurrence of the pigment locally and in the subpapillary regions

rather than deeper in the cutis." Wiedman expressed the belief that the pigment is for the most part in the macrophages, but that "the appearance in other cells is so similar to that of the pigment cells in the cancer masses that the conclusion cannot be escaped as to their neoplastic nature." Classifying the tumor among the tricho-epitheliomas, he stated that "indeed, it may be this very innate propensity for pigment formation in connection with hair formation that has determined the production of pigment in this case."

In our own cases and in other similar cases, it is conceivable that, with most of the pigment located in the chromatophores (this is phagocytosed pigment and was not formed by the chromatophores) of the cutis and very little in the tumor cells themselves, at some former time there was considerable pigment-forming activity of the basal cells; so much so, that the pigment overflowed the confines of its progenitors (the basal cells' dendritic melanoblasts), and, on wandering into the cutis, was phagocytosed and held by the chromatophores, a condition that would not likely occur unless an excessive amount of pigment were produced. Where the pigment elaborated by the basal cells is minimal or small in amount, it is quite conceivable that it would be retained by them.

The other alternative, that the basal cell epithelioma originated around clumps of nevoid pigment, is not borne out by histologic studies. Such a possibility, however, is suggested by the clinical history in both cases, e. g., the origin of what appeared to be a pigmented nevus, mole or birthmark.

In fact, the presence of pigment in such basal cell growths is viewed by Finnerud as substantiating the old theory of the nevoid origin of such tumors. With Nomland, he is shortly to report a case in which multiple epitheliomas arose in pigmented nevi.

PIGMENTATION IN TUMORS OTHER THAN MELANOMAS AND BASAL CELL EPITHELIOMAS

Both Masson and Caudière have extensively studied this phase of the subject. The latter,[14] in an interesting study concerning the evolution of pigmented cells in certain epitheliomas (notably cancers of the breast) which encroach on and invade the epidermis, made the following interesting comments:

1. In certain glandular epitheliomas of the breast encroaching on the epidermis one finds some pigmentary cells of the type of Langerhans cells.

2. These pigmentary cells come from the integument encroached on by the neoplasm. They emigrate by active ameboid motion downward to the neoplastic cords and are always strictly contained in the neoplastic epithelial loops. Their relationship to the neoplastic cells is a narrow symbiotic one, imitating their normal relationship to the cells of the deep layers of the epidermis.

3. By reason of the narrow relationship that the Langerhans cells have with the neoplastic elements, one can see some aspects that are not without analogy to those of certain nevo-epitheliomas. The tumors of the type under consideration, however, have nothing in common with the nevo-epitheliomas; they are tumors of glandular origin with pigmented symbiotic cells. Hence it is necessary to recognize this in order to avoid errors of interpretation. This is especially important in the interpretation of fragments (of tissue) taken for biopsy.

Masson,[16] too, has dealt with the pigmentation occurring in mammary cancers invading the epidermis. His conclusions are essentially the same as Caudière's (although Masson's work bears the stamp of priority).

Merenlender[17] has recently described some pigmented tumors of the skin under the title of "melanoblastoma parakeratodes." These tumors, apparently non-nevoid in nature, are comparatively benign and have a peculiar histologic structure, which does not in any way resemble basal cell epitheliomas associated with pigment.

DIFFERENTIAL DIAGNOSIS

In the differential diagnosis of basal cell epitheliomas with pigment from melanomas (melanocarcinoma), we believe that an absolute differentiation can be made only on histopathologic findings. Clinically, both of our own cases appeared to be melanomas; further, they both seemed to have originated in a pigmented nevus, and the lesions bled on trauma, which are reasons for believing the growths to be highly malignant.

From melanosarcoma, such lesions may be differentiated only by histopathologic studies.

From seborrheic keratoses[18] of the nevoid type, a clinical differentiation appears quite easy. Occasionally such keratoses are deeply pigmented, but only to the novice would a differentiation be difficult. Nevertheless, we have known cases of heavily pigmented keratoses to be regarded as melanomas.

Dermatosis papulosa nigra[19] is seen only in colored people, in whom melanomas and basal and prickle cell epitheliomas are exceedingly rare. Clinically, they have no resemblance to one another.

16. Masson, P.: La pigmentation des cancers mammaires envahissant l'épiderme, Ann. d'anat. path. **2**:322, 1925.

17. Merenlender, J. I.: Melanoblastoma parakeratodes, Arch. f. dermat. u. Syph. **162**:322, 1930.

18. Eller, J. J., and Ryan, V. J.: Senile Keratoses and Seborrheic Keratoses, Arch. Dermat. & Syph. **22**:1043 and 1050 (Dec.) 1930.

19. Michael, J. C., and Seale, E. R.: Dermatosis Papulosa Nigra, Arch. Dermat. & Syph. **20**:629 (Nov.) 1929.

Xeroderma pigmentosum presents a clinical picture quite distinct and unique. Basal cell epitheliomas arising in this disease, however, may contain considerable pigment (Montgomery).

Verrucous acanthotic nevi are often pigmented. In cases in which a clinical differentiation is difficult, a biopsy should be done. The section shows a typical histologic picture, as in figure 4.

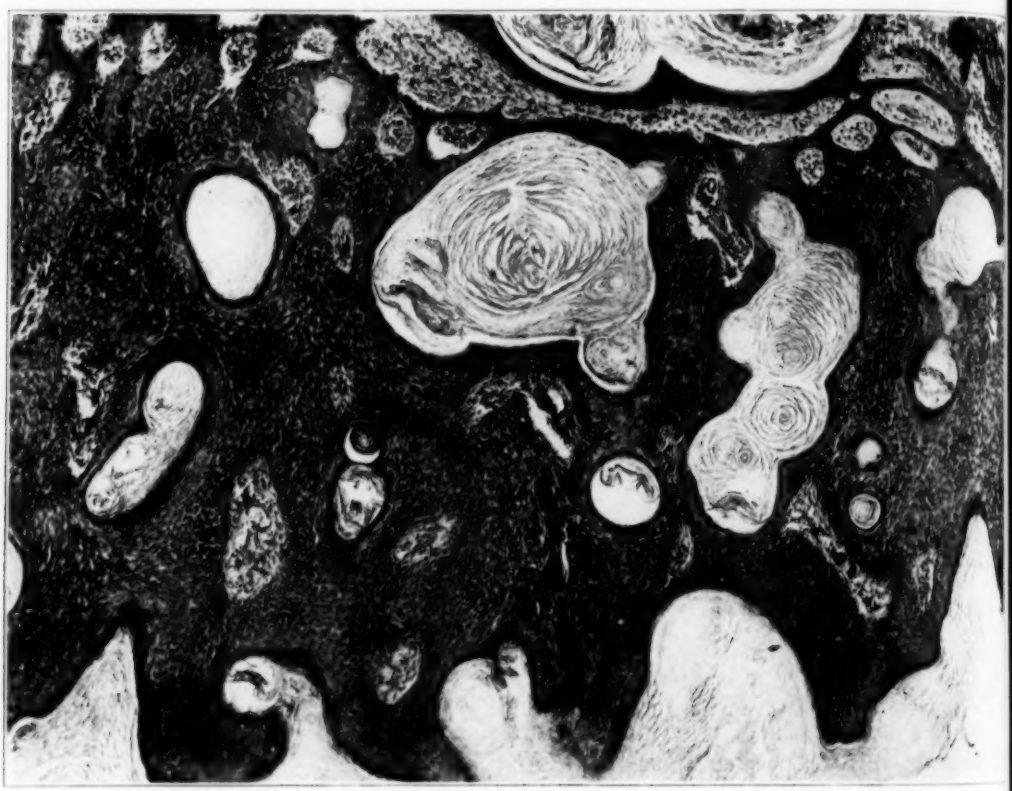


Fig. 4.—Verrucous acanthotic nevus with pigmentation.

TREATMENT

We believe the safest procedure to be thorough removal of all such pigmented growths by means of the endotherm knife, followed by heavy coagulation of the base. While we do not believe that the presence of pigment means that such basal cell epitheliomas are more malignant than the ordinary nonpigmented type, yet the cases so far studied and reported are too few to permit any conclusions as to their relative degree of malignancy. In all cases, whatever the treatment, the importance of saving an adequate amount of tissue for a thorough histologic diagnosis cannot be emphasized too strongly.

CONCLUSIONS

1. Two cases of basal cell epithelioma associated with marked pigmentation are reported.

2. The clinical similarity of such lesions to malignant melanoma is noted.

3. A clinical diagnosis of malignant melanoma requires a microscopic confirmation, as do also many cases of "typical" basal cell epithelioma.

4. Consideration is given to a group of epithelial growths involving the epidermis in which excessive or unusual pigmentation (melanoma) may be the predominating feature.

5. Pigment formation in malignant melanomas is of extreme practical importance. Pigment studies on other types of epidermal lesions, whether such lesions originate in the epidermis or originate elsewhere and invade the epidermis (as in cancers of the breast), may also be of value.

6. We prefer the term "basal cell epithelioma with pigment" rather than "benign melano-epithelioma of the skin" as suggested by Bloch. The inclusion of the term "melano" as advocated by Bloch is technically correct. However, epitheliomas are not in any sense "benign," and the term "melano-epithelioma" at once brings to mind the most malignant of skin tumors, the melanomas.

100 West Fifty-Ninth Street.

2007 Wilshire Boulevard.

CUTANEOUS HYPERSENSITIVITY TO MERCURY FROM TATTOOING

REPORT OF A CASE

D. B. BALLIN, M.D.
NEW YORK

Cutaneous sensitivity to mercury and its compounds is relatively frequent. However, its manifestation two years after a tattoo was made, as in the case described, seems unique and warrants this report. My search of the literature does not reveal any exactly similar case.

P. Unna, Jr.,[1] in 1930, reported the case of a 63 year old man who had been tattooed in his youth and who acquired syphilis at the age of 43. In the treatment for this disease he received mercurial inunctions, which gave no trouble. Following dermatitis induced by the application of mercury for the treatment of hemorrhoids, itching, swelling and vesicles ranging in size from that of a pinhead to that of a pea developed in the red (cinnabar?) part of the tattoo. The india ink part of the tattoo was unaffected. A patch test made with mercurial plaster gave a positive reaction.

In my case, no precipitating cause other than the tattoo could be found.

REPORT OF A CASE

A man, aged 20, who came to the clinic on Aug. 5, 1931, complained of a condition which had been present for two months. A history of contact with an irritant could not be obtained. The patient had been unemployed for several months. The tattoo had not given any trouble for two years after it was made. For the past two months, the red parts of the tattoo had been itching, swollen and oozing. The condition varied in intensity, but was constantly present. Tiny vesicles would form and rupture, leaving oozing, smarting, raw areas over which thin, yellowish, friable crusts appeared.

The tattooed area was on the middle third of the extensor surface of the left forearm. It consisted of two overlapped hearts in red and outlined in blue. The middle third of this design was a strip of normal skin in which the words "true love" were tattooed in blue. On the radial side, below, and on the ulnar side, above, was a forked ribbon in red and outlined in blue. Below the hearts were the words "to mother." Above the hearts was a leaf design in blue, and in the middle of it, a flower in red and outlined in blue. The red parts (cinnabar?) were swollen and oozing and in places thinly crusted. In one place, the remains of vesicles could be seen (accompanying figure). The blue areas showed no evidence

---

From the Outpatient Department of the Mount Sinai Hospital Clinic of Dr Max Scheer, service of Dr. Walter J. Highman.

1. Unna, P., Jr.: Arch. f. Dermat. u. Syph. **160**:153, 1930.

of inflammation. Examination of the rest of the skin showed nothing except a slight tendency to seborrhea. The general health had always been good, and physical examination gave negative results. Several specimens of urine were examined and were found to be negative for signs of renal disease. The patient stated that he had never taken mild mercurous chloride.

A 2 per cent ointment of ammoniated mercury was applied to the flexor surface of the other forearm, and in twenty-four hours the area to which the salve had been applied under a nonocclusive dressing was red and swollen. Thirty-six hours later the area was a sheet of closely set tiny vesicles which broke, leaving a moist surface which crusted with dried serum. It was about two weeks before the skin was normal again.

On another area on the flexor surface of the right forearm, a patch test with a 1:1,000 solution of corrosive mercuric chloride was made when all traces of the first patch test had disappeared, and in twenty-four hours the skin was itching, reddened and swollen. Vesicles did not appear, but the redness and swelling lasted

Forearm of patient showing sensitivity to mercury as a result of tattooing.

more than a week. Patch and scratch tests made with cinnabar at the same time gave negative results.

It was suggested to the patient that it might be possible to relieve his condition by removing the affected areas. With his consent, this was done with the punch, which usually penetrated to the fat. In one area on the radial side, a nerve branch was encountered, and here the punched portions were snipped off more superficially. A piece of tissue was saved for histologic examination. The report by Dr. Samuel M. Peck was as follows:

"There is seen in one portion of the slide a great deal of black, amorphous pigment which is lying free in the tissue in scattered clumps in the papillary and subpapillary layers of the cutis. In the unstained slide, the periphery of such an amorphous mass shows red granules. The epidermis directly over this pigment is acanthotic and shows finger-like projections into the cutis. There is a moderate amount of spongiosis. Surrounding the pigment mass are diffuse areas of cellular infiltration consisting of large round cells, a few polymorphonuclear leukocytes, eosinophils, and plasma cells. The blood vessels in this inflammatory area are dilated and filled with blood. A similar clump of pigment is seen deep in the cutis below the area described above and shows a similar surrounding cellular exudate.

The epidermis extending away from this area gradually returns to normal and at one point there is seen in the subpapillary layer, an amorphous mass of black pigment which shows no inflammatory reaction. This is probably a black tattooing."

The punched-out areas were allowed to granulate inward, and the patient was kept under observation. After the areas had been filled with scar tissue, they continued to manifest the same condition that had existed before the punch was used. There occurred redness and swelling of the affected parts, with the formation of fissures or blebs which ruptured, affording the patient temporary relief. When the patient was last seen, the condition was unchanged, and he did not comply with later requests to return to the clinic.

COMMENT

According to the United States Dispensatory, the chemical properties of cinnabar are as follows: It is insoluble in water, strong acids and dilute alkalis. However, from observations recorded in the literature and in the case herein reported, it is obvious that sufficient active mercury is sometimes present in cinnabar to react with the human tissues. In this case, there is a possibility that such small traces of the element may have caused the sensitization.

SYSTEMIC PHASE OF TUBERCULOSIS CUTIS

ELMORE TAUBER, M.D.
AND
LEON GOLDMAN, M.D.
CINCINNATI

Tuberculous involvement of the skin is an interesting part of the picture of tuberculosis. Any observations that bring illuminative information to the old problems of tuberculosis of the skin should be welcomed. This is possible to some extent when easily recognizable foci in other organs are present. The interest is increased further when the tuberculosis of the skin is in the Negro. Because of the comparatively recent invasion of the Negro race by the tubercle bacillus and the consequent preponderance in that race of the "puerile" form of tuberculosis, a study of the involvement of the skin may contribute something to the confusing mass of "allergy," "anergy" and "resistance." Tuberculosis cutis is still relatively uncommon in the Negro. Jones [1] stated that: "Although lupus erythematosus and various tuberculids are not uncommon during tuberculosis of the skin, lupus vulgaris in our section of the country is almost unknown."

The following few cases were successive ones of tuberculosis cutis observed in the medical and dermatologic services of the Cincinnati General Hospital. The general physical examination in each instance was made by Dr. Roger S. Morris.

REPORT OF CASES

CASE 1.—*History.*—A. M., a colored woman, aged 47, a cook, noted the eruption about three years prior to admission to the hospital. It began as small "bumps" around the eyes and cheeks, and later appeared on the hands. Some of the lesions disappeared apparently spontaneously. Later the patient received intramuscular and intravenous therapy, without any appreciable effect on the lesions. Various types of local cauterization were used on the lesions of the hands. At this time, the Wassermann reaction of the blood was negative. For about ten years the patient had noted small swellings about each elbow; she believed that her mother had similar swellings about the elbow. The patient complained also of substernal pains; there was no dysphagia or dysarthria. There seemed to be a gradually increasing dyspnea on effort. There was no history of congestive heart failure. There were vague epigastric pains associated at times with nausea

From the University of Cincinnati, College of Medicine, and the Department of Dermatology, Cincinnati General Hospital.

1. Jones, J. W., in discussion of Allison, T. R., and Mikell, P. V.: Sarcoid Associated with Tuberculosis of the Larynx, Arch. Dermat. & Syph. **25**:334 (Feb.) 1932.

and emesis. The patient had had a large subcutaneous "fatty tumor," removed from the left lumbar region eight years before admission to the hospital. A fibroid tumor had been removed in 1923. The only pregnancy, which had occurred many years previously, resulted in a miscarriage. There was no known history of pulmonary, glandular or osseous tuberculosis. There had been fairly prolonged contact with a tuberculous cousin. "Scrofula" had been present extensively on the maternal side of the family.

Examination.—The patient did not appear acutely or chronically ill. There was no dyspnea, cyanosis, icterus or petechiae. The skin was warm, moist and elastic. Small pigmented areas were scattered over the thorax. In the left lumbar region

Fig. 1 (case 1).—A Negro woman with tuberculosis cutis.

there was a linear scar with a slight keloidal reaction. The eruption was confined chiefly to the face, neck and hands. The lesions consisted of small, discrete and confluent papules and nodules. The papules were most numerous about the eyelids, nares and lips; about the nares they had a mulberry appearance. Diascopic pressure showed apple-jelly nodules. The scarring of the lesions around the terminal phalanges gave the fingers a clubbed appearance. A few small circular scars were seen over the anterior part of the thighs. There was adenopathy involving the axillary, epitrochlear and inguinal regions; the epitrochlear glands were especially prominent, being 6 cm. in diameter. There was, curiously, no cervical adenopathy. Otherwise the physical examination gave entirely negative results.

The blood count revealed: white cells, 6,700; red cells, 4,300,000, with 90 per cent hemoglobin. A differential count showed: lymphocytes, 22 per cent; large mononuclears and transitionals, 7 per cent; polymorphonuclear leukocytes, 70 per cent, and eosinophils, 1 per cent. Urinalysis showed an alkaline reaction to methyl red; the reaction to albumin was 1 plus, and the reaction to sugar, negative. The results of a microscopic examination of the urine were negative. The Wassermann test of the blood was negative on two occasions. The blood sugar was 105; urea nitrogen, 9, and carbon dioxide, 58 mg. per hundred cubic centimeters. The reactions to human and bovine tuberculin given intradermally were negative. Nasal smears showed no acid-fast bacilli. Roentgen examination of the chest was made

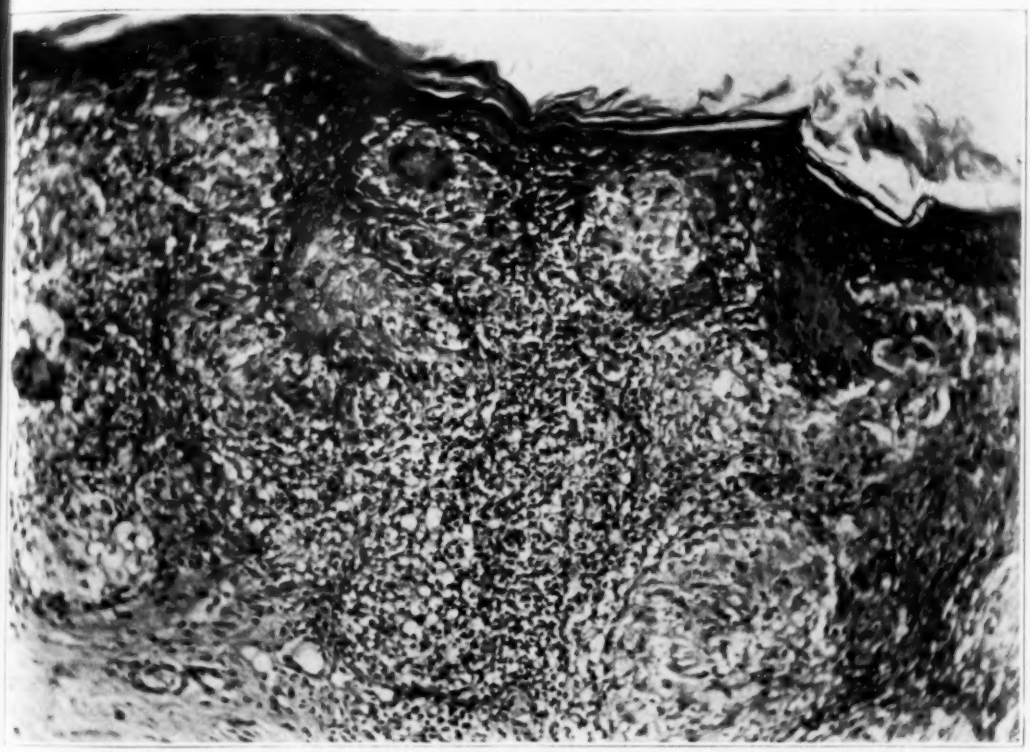


Fig. 2.—Fibrosis and typical tuberculous structure; note the giant cells.

by Dr. Harold G. Reineke, who made the following report: "A circular area of increased density lies just to the right of the midline behind the sternum, between the second and fourth ribs. The shadow is homogeneous throughout and has regular contours; it measures 3 by 5 by 5 cm. Two additional circular areas of similar density, measuring about 3 cm. in diameter, lie in the region of the right hilus and slightly below it. There is thickening of the interlobar pleura in this region. There is another circular density adjacent to the spine on the left in front of the eleventh rib. The right side of the diaphragm is irregular and is sharply elevated through its middle third. Reexamination of the chest about seven months later showed no appreciable changes."

Pathologic Report.—Biopsy was permitted only on a portion of the skin from the left cheek and on the right epitrochlear gland. On gross section, this gland was found to be light brown, homogeneous throughout and firm. Inoculation of material from this gland into animals was not done. The microscopic sections were studied by Dr. Alfred E. Glazer of the department of pathology. His report was as follows:

"Skin: The dermis presents a barely microscopic conglomerate tubercle which extends from the epidermis to the subcutaneous fat and is composed of a number of small tuberculous areas. The predominating cells of these tubercles are endothelial leukocytes, groups of which are radially arranged about the centers of the small tubercles. Together with endothelial leukocytes there are occasional lymphocytes and a few giant cells. These small tubercles in turn are surrounded by a few circularly placed fibroblasts. In other areas within the large tubercle, endothelial leukocytes are intermingled with edematous fibroblasts and arranged in a medullary manner. In still other areas within the large tubercle there are irregular foci of scattered pyknotic lymphocytes lying in a loose areolar tissue network. The entire tubercle is surrounded by a rather dense band of elastic tissue together with an occasional lymphocyte. The epidermis in this region is atrophic and the basement membrane is indistinct in many places. The prickle cell layer is much thinner than normal.

"Lymph Node: The normal architecture is practically entirely replaced by discrete or confluent loosely packed nests of endothelial leukocytes and fibroblasts without a consistent type of architecture. Associated with these cells there are occasional lymphocytes, but there is no evident necrosis. A few giant cells are seen. These nests of cells are partially surrounded by loose bands of elastic fibers together with numerous lymphocytes. In other areas, the lymph node presents diffuse fibrosis, and in some of these areas the fibers appear to be undergoing hyaline degeneration."

Case 2.—*History.*—I. M., a colored man, aged 27, a laborer, complained of an eruption about the nose and lips which had appeared one year prior to admission to the hospital. For the past four years he had noted large, irregular swellings in his neck. No cough, pleuritic pains or night sweats had been present. There had been no loss of weight. There was no known history of syphilis, or of pulmonary, glandular or osseous tuberculosis.

Examination.—On the patient's admission to the hospital, examination revealed a well developed and well nourished young colored man who appeared neither acutely nor chronically ill. The temperature was 98 F.; the pulse rate, 78; the respiratory rate, 20, and the blood pressure, 112 systolic and 72 diastolic. The skin was moist, elastic and clear, save for an eruption over the face and neck. The lesions consisted of small reddish-brown, discrete and confluent papules, gathered about the eyelids, nares and angles of the mouth. Diascopic pressure showed apple-jelly nodules. No lesions were seen in the vestibule of the nose or on the buccal mucosa. Large matted glandular masses were scattered throughout the cervical triangles. Enlarged discrete epitrochlear and axillary glands were present. The inguinal glands were palpable, but not especially enlarged. The remainder of the physical examination gave negative results.

The cell count showed: white cells, 9,300; red cells, 4,800,000, and hemoglobin, 85 per cent. A differential smear showed: lymphocytes, 31 per cent; polymorphonuclear leukocytes, 59 per cent; eosinophils, 2 per cent; basophils, 1 per cent, and large mononuclears and transitionals, 7 per cent. The urine was normal. The Wassermann test of the blood was negative. The reaction to human and bovine tuberculin was negative. A roentgenogram of the chest showed ovoid areas about

the bifurcation of the trachea; these areas doubtlessly represented large glands. A gland from the neck and a portion of the skin of the upper lip were removed for biopsy. The pathologic report by Dr. Glazer was as follows:

"Lymph node: The normal architecture of practically the entire node is replaced by multiple discrete and confluent tubercles of varying sizes.

"Skin: The upper portion of the dermis presents discrete and confluent tubercles of varying sizes. Some of the larger tubercles have caseous centers. The remainder of the dermis is infiltrated densely with elastic and collagenous fibers. The prickle cell layer of the epidermis overlying the tubercles is thinner than normal."

CASE 5.—*History.*—J. F., a colored man, aged 30, a porter, was admitted to the hospital complaining of dyspnea on effort of about one year's duration. There was an infrequent cough productive of mucoid sputum. He had no pleuritic pains, night sweats, hemoptyses of any degree or loss of weight. The patient had been hoarse for ten years, "following burning of his tonsils with a needle." Three or four months prior to his admission to the hospital, small "bumps" were noted about his nose, eyelids and lips. The patient also gave a history of frequent penile lesions, which consisted of small pruritic "bumps" (vesicular?). There had not been buboes or previous eruptions. The patient said that tests of his blood for syphilis were positive several months previously, but he had not received intravenous or intramuscular therapy. The patient's wife had been taking "shots" since the birth of their last child, three years previously. There was no family or personal history of any form of tuberculosis. The patient had worked only as a porter, chauffeur and errand boy.

Examination.—Examination on admission revealed a young colored man who appeared to be neither acutely nor chronically ill. The temperature was 98 F.; the pulse rate, 80, and the respiratory rate, 20. The voice was hoarse. There was an eruption of copper-colored, flat, papular lesions over the eyelids, about the nares and the angles of the mouth, under the chin and over the back of the neck. These lesions varied in size from that of a pinpoint to that of a pea. The only glands that were palpable were a few shotty cervical and small inguinal nodes. An examination made by Dr. Kully of the nose and throat service showed large tonsillar remnants in both fossae; two large healed midline perforations of the palate, and interarytenoid infiltration with fine ulceration of both true vocal cords. Dr. Kully's diagnosis was tuberculous laryngitis. The trachea was in the midline. There was some impairment of expansion of the left side of the chest. The percussion note was resonant throughout; the breath sounds were fairly intense, with bronchovesicular breathing at the right base posteriorly and crepitant râles on both sides from the base to the angle of the scapula. The remainder of the physical examination revealed no relevant details.

Laboratory and Roentgen Reports.—The white cells numbered 7,300 and the red cells, 6,200,000; the hemoglobin was 80 per cent. A differential smear showed: lymphocytes, 9 per cent; large mononuclears and transitionals, 19 per cent; polymorphonuclear leukocytes, 64 per cent; eosinophils, 7 per cent, and basophils, 1 per cent. The urine was normal. The Wassermann test of the blood was positive. The sputum showed acid-fast bacilli.

Dr. Reineke made the following report on the roentgenograms: "X-ray examination of the chest in the sagittal and lateral views shows enlargement of the mediastinal shadow to the right and exaggeration of the area of the aortic notch on the left. The heart is normal. Extensive diffuse fibrosis is present throughout both lungs, the changes being most marked in the hilus and bases. In the tops, where these lesions are seen, they are quite characteristic of an acid-fast process.

When seen from the side there is some dilatation of the aortic notch. Considerable infiltration is present in the posterior mediastinum. These findings are in addition to those recognized in the anteroposterior views. Conclusions: Moderate dilatation of the aortic notch; the pulmonary changes are likely those of tuberculosis with associated tuberculous adenopathy in the mediastinum."

In the report on the microscopic section taken from a portion of the skin from the lip, Dr. Glazer noted that there were "two definite tubercles in the upper portion of the dermis with a small, eccentric focal area of necrosis in the larger tubercle."

COMMENT

These three cases, then, show tuberculosis cutis associated with glandular tuberculosis and, in case 3, with pulmonary and laryngeal tuberculosis. The cutaneous lesions appear to be of lupus miliaris disseminatus.[2] The lesion of the hand in case 1 may be considered by some as an associated sarcoid type. However, lesions on the extremities do occur in lupus miliaris disseminatus,[2c] and the keloidal reaction associated with repeated attempts at cauterization may have produced the nodular form that was evident. Lupus miliaris disseminatus is an uncommon disease of the skin according to the general medical literature, although relatively more cases are described in dermatologic literature.[3] There are, however, practically no statistics available in regard to the frequency of lupus miliaris disseminatus in the Negro.

Further analysis of these cases shows some rather interesting details. Although there is a large personal factor in the patient's history in case 3, glandular swellings preceded evident lesions of the skin and respiratory complaints were noted before the cutaneous manifestations. These facts, associated with the pathologic picture, may add further evidence to the hematogenous development of this form of lupus. The onset of the eruption in each case was apparently not associated with acute symptoms. All three patients showed glandular tuberculosis and, especially, mediastinal involvement. The association of tuberculosis of the skin with tuberculosis of other organs is supposed to be infrequent.[4] The percentages usually given are from 2 to 8. From a study of tuberculosis of the skin in children, in whom this condition is more common than in adults, Bruusgaard believes that the condition occurs

2. (*a*) Wise, F., and Satenstein, D. L.: Clinical and Histologic Features of Certain Types of Cutaneous Tuberculosis, Arch. Dermat. & Syph. **4**:586 (Nov.) 1921. (*b*) McCarthy, Lee: Histopathology of Skin Diseases, St. Louis, C. V. Mosby Company, 1931. (*c*) Volk, Richard: Tuberkulose der Haut, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 10, pt. 1.

3. (*a*) Volk.[2c] (*b*) Peck, Samuel: Beitrag zur Lehre von Lupus miliaris disseminatus faciei, Arch. f. Dermat. u. Syph. **158**:545 (Oct.) 1929.

4. Fischl, Friedrich: Die Hauttuberkulose als Organsystemerkrankung, Wien. klin. Wchnschr. **36**:611 (Aug.) 1923. Christie, J. F.: The Association of Skin Tuberculosis with Visceral and Other Tuberculous Manifestations, Brit. M. J. **2**:551 (Oct.) 1921.

after bronchial and glandular tuberculosis, and that it is more difficult to find the primary focus as the child grows older.[5] When one considers the extent of tissue invasion in such cases one is struck by the apparent mildness of the reaction. A negative reaction to tuberculin (1 : 1,000) given intradermally, as occurred in two cases, has been noted before in lupus miliaris disseminatus.[3b] In each case, moreover, the cutaneous picture aided materially in the diagnosis of the patient's condition. Conversely, the necessity for a complete careful examination of the patient with tuberculosis cutis is shown.

In regard to local treatment, complete excision, electrocoagulation and electrodesiccation were performed. During the brief period of observation of these cases the spontaneous disappearance of lesions was not noted.

CONCLUSIONS

1. Three cases of tuberculosis of the skin in Negroes, of the lupus miliaris disseminatus type, were associated with glandular tuberculosis, especially prominent mediastinal tumors, and in one case with far advanced pulmonary and laryngeal tuberculosis.

2. In spite of the extensive tuberculosis, a relatively benign appearance was noted.

3. The necessity for complete examination of a patient with tuberculosis cutis is shown as the solution of the problem of therapy for the individual patient is only begun with the recognition of the cutaneous phase of the condition.

---

5. Bruusgaard, E.: Tuberculosis of the Skin in Children and Its Importance, Comp. rend. VIII Cong. internat. de dermat. et syph., 1930; abstr., Brit. J. Dermat. & Syph. **44**:101 (Feb.) 1932.

ACNE CONGLOBATA

AN EXPERIMENTAL STUDY

GEORGE H. BELOTE, M.D.
Associate Professor in Dermatology and Syphilology, University of Michigan Medical School
ANN ARBOR, MICH.

Previous to the study by Michelson and Allen,[1] practically all the literature on so-called acne conglobata concerned itself with the minutiae of clinical and pathologic description, with a discussion as to its relationship to other pyodermias, and with the attempt to fasten on it a tuberculous etiology. Because of the shortness of time and because this literature has little in common with this experimental study, other than in name, only two previous publications will be reviewed. For the bibliography on the subject, the interested reader is referred to the study mentioned.

In 1924, Strumia[2] published a report, under the name "Experimental Acne Varioliformis," of experimental work carried out in a case of chronic, resistant pyodermia. From the clinical description, this case does not quite fit acne conglobata, but I believe that it is closely related and, in view of this work and that published by Michelson and Allen,[1] the findings and conclusions of Strumia are of interest. He was able to reproduce typical lesions by intradermic injections of the staphylococci and streptococci found in his case, but he also found that he could obtain the same result by the use of stock organisms of a similar type. He concluded that the organisms found were not specific for the disease. This is referred to particularly because it apparently has been missed in previous reviews and because the results are closely similar to mine.

The other study which I wish to review briefly is that of Michelson and Allen.[1] It furnished the stimulus for this work.

In an undoubted case of acne conglobata these authors found that they were able to reproduce typical lesions in the patient by intracutaneous or subcutaneous injections of pus from other lesions or of

---

Read at the Fifty-Fifth Annual Meeting of the American Dermatological Association, Havana, Cuba, May 3, 1932.

Studies and Contributions of the Department of Dermatology and Syphilology, University of Michigan Medical School, Service of Dr. Udo J. Wile.

1. Michelson, H. E., and Allen, P. K.: Acne Conglobata, Arch. Dermat. & Syph. **23**:49 (Jan.) 1931.

2. Strumia, Max M.: Experimental Acne Varioliformis, Arch. Dermat. & Syph. **10**:702 (Dec.) 1924.

the purified staphylococcus which was constantly found present. However, they were unable to produce lesions in any other subjects, either normal or suffering from severe acne vulgaris, nor were they able to produce lesions in the patient by using organisms from other cases of acne vulgaris.

From this study it seems obvious that the authors were not dealing with a specific organism in the sense of one wholly responsible for the disease; otherwise it should have produced lesions in the control patients. Yet, they were unable to produce lesions by the use of other organisms of the same type, and this would seem to indicate a certain specificity for the patient's own organisms. It would seem justifiable to conclude that they were dealing with a combination of specific organisms in a highly unusual patient, although Michelson doubted this specificity.

These results contrast rather sharply with those of Strumia [2] in another closely similar case. He found the organisms distinctly nonspecific, and this refers the unusual portion of the condition to the patient himself. Unfortunately, no human experiments other than on the patient were carried out, although the lesions were repeatedly reproduced in experimental animals.

REPORT OF CASES

Because of lack of space, I shall not enter into a long history and clinical description of my two cases. The diagnosis is obvious from the photographs. Points of interest and importance in the histories and examinations are as follows:

CASE 1.—A man of 42 years gave a history of widespread recurrent lesions since the age of 12. The early lesions he regarded as similar to those present. He was first seen in this department in 1919, and at that time a considerable discussion arose as to a possible tuberculous or syphilitic etiology. The Wassermann test continuously gave negative results, as did inoculations of guinea-pigs carried out in the attempt to establish a diagnosis of tuberculosis. After about one year of observation and treatment of various kinds, the condition cleared up, and the patient had no more trouble for ten years. He reappeared at the clinic in May, 1931, and his condition was as shown in figure 1. The Kahn test at this time was negative, a roentgenogram of the chest showed no evidence of tuberculosis, and all cutaneous tests with human, bovine and avian tuberculin gave negative results. Mycelia were not found. The only unusual findings aside from the skin were a palpable spleen and a persistent but mild albuminuria.

CASE 2.—A man of 20 years dated the onset of his difficulty from about five years before. The eruption began on the face, but soon spread to involve most of the body. Except for mild remissions, the eruption had been constantly present, and at the time of his first examination in October, 1931, he presented the picture shown in figures 1 and 2. In addition to the widespread eruption, he showed a distinct acne vulgaris in the usual distribution, and his skin was of a seborrheic variety. Comedones were not as much in evidence as in case 1. The Kahn test of the blood gave negative results, roentgenograms of the chest were not more

than slightly suggestive, and tuberculin tests with human, bovine and avian tuberculin gave negative results. Inoculations of guinea-pigs were not performed. A general physical examination revealed only oral sepsis and an alveolar abscess. The pathologic report on an excised lesion is as follows: "Subacute purulent process with pustule formation. Hyperplasia of the epidermis with excessive cornification within the hair follicles and at the mouth of the sebaceous glands. Foreign body giant cell reaction, apparently associated with the destruction of the sebaceous gland which forms the center of the pustular process. This specimen

Fig. 1.—The patients in case 1 (right) and case 2 (left), showing widespread lesions and marked scarring.

gives the impression that the underlying pathology is an anomalous and excessive accumulation of keratohyalin in the mouths of the hair follicles."

At the time the second patient entered the hospital the condition of the first patient had practically cleared up; no new lesions were developing at this time, and he presented only a mild activity in a few old ones. Before the experimental work could be carried far, he was forced to leave the hospital. Consequently, except when noted, the experimental work applies only to case 2.

Before presenting this material I wish to define three terms as here used. 1. Negative results: Either no lesion was produced or one which disappeared in three or four days. 2. Positive results: The lesion produced remained active at

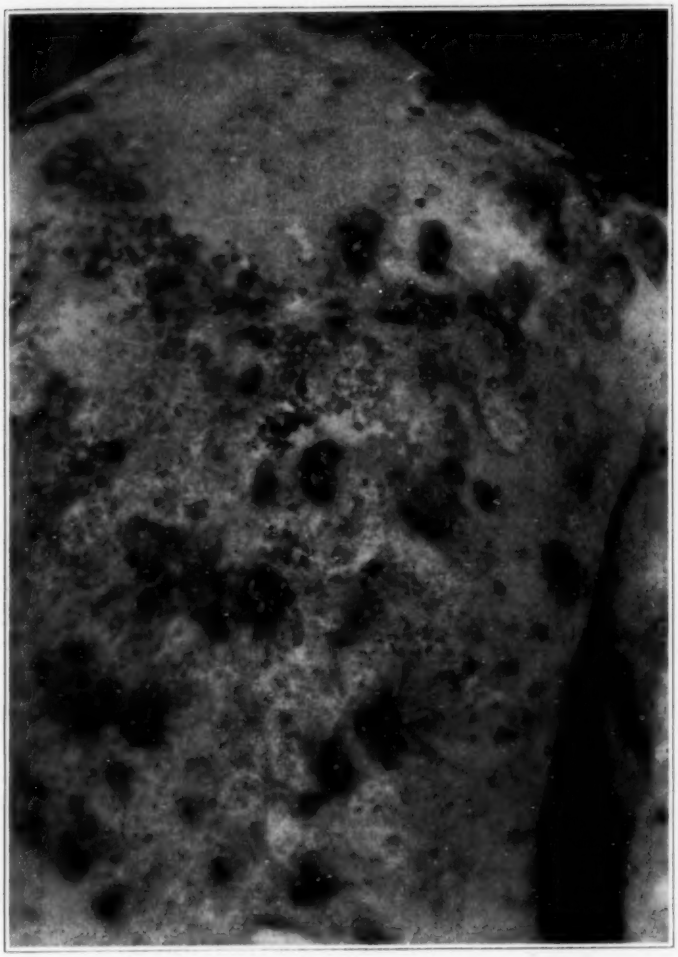


Fig. 2.—Back of patient in case 2.

Fig. 3.—Lesion produced by cross-inoculation from case 1 to case 2. The material used was pus from a lesion opened aseptically.

least three weeks, and simulated in miniature the original lesions. 3. Controls: Each experiment was controlled by similar injections into three other patients of the type desired for that particular experiment.

SUMMARY AND EXPERIMENTAL DATA

Cultures of the blood gave persistently negative results in both cases.

The organisms found were as follows: In case 1, Staphylococcus aureus was constantly present in all closed lesions opened aspetically. Streptococcus haemolyticus was found on one occasion. Bacillus acnes was also found on one occasion. B. coli was found in open lesions only. In case 2, Staphylococcus albus was constantly present in all lesions opened aseptically. B. coli was found in open lesions only.

The cutaneous reaction to material other than living organisms was as follows: to sterile broth, negative results in both cases and in the controls; to sterile saline solution, negative results in both cases and in the controls.

No agglutinins were found in either case for those organisms constantly present in lesions opened aseptically.

Cross-inoculation gave positive results from case 1 to case 2, but negative results from case 2 to case 1. All controls showed negative results. At this time the first patient was forced to leave the hospital. He had no active lesions remaining.

Auto-inoculation with pus from another lesion gave positive results in case 2 and negative results in the controls; with autogenous Staphylococcus albus, positive results in case 2 and negative results in the controls.

Results of inoculation with other organisms in case 2 were: with the Gratia strain of Staphylococcus albus, positive results; with Staphylococcus aureus from another patient, positive results; with B. coli, negative results. The results in all the controls were negative.

Broth filtrates of Staphylococcus albus from the patient in case 2 and the Gratia strain of Staphylococcus albus both produced in this patient a marked cutaneous reaction of an erysipeloid type, accompanied by marked pain, which, however, subsided in seventy-two hours. The reactions in this subject and the controls were indistinguishable.

In case 1 the phagocytic power of whole blood was approximately equal to that in the controls. In case 2 it was high—well above the average of the controls.

In case 2 inhibition of the growth of the patient's own organisms in whole blood was marked, up to nine hours. There was distinctly more inhibition than in the blood of the controls. The blood serum in case 2 showed no greater inhibition than the serum of the controls.

Three months after the patient in case 1 was discharged, he returned to the hospital for a short time. At this time he presented no active lesions, and during a month of observation only two small lesions developed, which subsided promptly. He still had the marked seborrheic type of skin, and comedones were much in evidence. I took this opportunity to inoculate him both intracutaneously and subcutaneously with a culture of his own staphylococcus, with the Gratia strain of the white staphylococcus, with a yellow staphylococcus from another patient and with the acne bacillus isolated from the patient himself. Injections were made into the arm, the leg and old scars on the back. In no case was I able to reproduce a lesion, although at this time the patient again showed no agglutinins for the staphylococci used.

COMMENT

The constant finding of staphylococci in all closed lesions is in accord with practically all previously published work, although the question of the rôle of tuberculosis has arisen on various occasions. The white type of staphylococcus seems to be the more common, although the yellow type was ultimately reported by Clawson and Allen [3] in the case published by Michelson and Allen.[1] In my cases the yellow type was found in the first and the white type in the second. The other organisms reported were inconstantly found and regarded as incidental.

The lack of agglutinins in the patient's blood serum for those staphylococci which were constantly found is also in accord with the previously published articles. Michelson regarded this as the key to the whole situation, but I found no agglutinins even after the lesions had cleared up.

That simple trauma was not sufficient to produce lesions in these patients is evidenced by the lack of response to the intracutaneous injections of sterile broth and sterile saline solution. Sterile filtrates of staphylococci, prepared according to the standard technic, produced marked local reactions which subsided in seventy-two hours. In this case, however, the reactions in the controls were identical with those in the patient himself.

As far as I know, this is the first report of pus from one patient with acne conglobata being inoculated into another patient with a case of the same type. Even though the organism isolated from the patient in case 1 was a yellow staphylococcus, this pus, which may have also contained streptococci and B. coli, produced a fairly typical lesion in case 2. This seemed to me important, because the predominating organism in case 2 was a white staphylococcus. Cross-inoculation from case 2 to case 1 gave negative results, but one must remember that in case 1 the condition had practically cleared up at that time.

The experiments on auto-inoculation merely repeat and confirm the findings of Michelson. I was able to reproduce lesions by intracutaneous injections of either the pus from another lesion or the purified Staphylococcus albus found in case 2. However, the positive results obtained on inoculating the second patient intracutaneously with the Gratia strain of Staphylococcus albus and with a yellow staphylococcus from a nasal secretion are not at all in accord with the previously reported findings. Michelson and Allen were unable to reproduce lesions except by using organisms from the patient himself. Attempts with B. coli and B. acnes also gave negative results.

---

3. Clawson, B. J., and Allen, P. K.: Intravenous Vaccine Therapy in Staphylococcic Infections, Arch. Dermat. & Syph. **23**:894 (May) 1931.

The ability of the first patient to phagocytose his own organisms and those of the second patient was not remarkable. Case 2, on the other hand, showed a phagocytic ability well above the average of the controls.

Inhibition of growth of organisms was not carried out in case 1. In case 2, however, the whole blood showed a marked inhibition of growth, while the blood serum showed no ability to inhibit growth greater than that of the controls. This finding probably is dependent on the phagocytic ability of the whole blood, and might lead one to speculate as to what might happen to this patient if it were not for his phagocytic ability.

It seems to me that the one outstanding fact from this work and all that has gone before is that no one has been able to reproduce a lesion simulating acne conglobata in a person not already affected. Since the organisms constantly found in lesions opened aseptically have been used and the lesions have been reproduced in the patient himself but not in controls, it follows that the organism present is not specific in the sense that the diphtheria bacillus is specific for diphtheria or the typhoid bacillus specific for typhoid fever. For this reason, and since it was possible to produce lesions by using other organisms, it is obvious that the only other possible factor is the patient himself.

From the work of Michelson and Allen, it appeared that the condition rested on a combination of a specific organism plus a susceptible patient. The additional data from my work seem to leave out the necessity for a specific organism and require only an unusual person. I was able to get positive results in a highly active case with all the pus-forming organisms tried. In a case that was inactive, however, I was unable to get a positive result with any organism, regardless of the point or depth of inoculation.

That the positive result is not due to trauma or to toxic products of the organisms is shown by the lack of response to broth, saline solution and broth filtrates.

That the patient in case 2 is unprotected as regards agglutinins is obvious from this study and that which has gone before. However, that a lack of agglutinins cannot be held responsible for his condition also is obvious from the fact that he had none when the lesions entirely cleared up. Furthermore, his blood serum showed no marked inhibition of growth. The one redeeming feature seems to be his rather marked ability to phagocytose his own organisms.

From the combined study of these two cases, the following conclusions would seem justified:

1. Tuberculosis as the specific etiologic factor can be excluded.

2. Except ordinary pus-forming organisms, no bacteria were constantly found in closed lesions.

3. Specific agglutinin reactions were not found for the staphylococci constantly present while the cases were either active or inactive.

4. The condition apparently is not caused by a specific organism.

5. The etiologic factor of importance apparently is the patient himself and involves a constitutional predisposition.

6. Depending on the stage when the case is seen, experimental data may vary considerably.

Laboratory assistance was given by Mr. C. B. Stapleton of the University Hospital Clinical Laboratories.

ABSTRACT OF DISCUSSION

Dr. Fred D. Weidman, Philadelphia: The work of Dr. Strumia which has been alluded to was performed in my laboratory a number of years ago, and the patient was shown at a meeting of the Philadelphia Dermatological Society. It was there that Dr. Knowles proposed the diagnosis of acne varioliformis, which we thought was best for the case. I think that the terms "acne conglobata," "acne cachecticorum," etc., are not to be quibbled about. The outstanding question with us was whether the cause of the lesions was the tubercle bacillus. We isolated staphylococci and streptococci and inoculated the patient with (1) the streptococcus, (2) smallpox vaccine, (3) some of the pus, (4) a mixture of the staphylococcus and the streptococcus, (5) physiologic solution of soduim chloride (control) and (6) turpentine. We tried these different types of irritants to see if we could reproduce the type of lesions present in our patient. With materials 1, 3 and 4 we got classic lesions. One of the spontaneous lesions (control) compared well indeed with the lesion induced by mixed staphylococcus and streptococcus strains. These results agree with the ones reported today by Dr. Belote; i. e., the tubercle bacillus is not necessary for the production of this type of lesion, and a particular strain of organism is not necessary. It appears to be established now that the patient is the factor in determining the special kind of reaction that takes place in these cases. In fact, one must think of the two sides of the shield in every dermatologic case, the particular type of organism and the particular type of reaction given by the patient. It may be that future work will map out even more accurately and fully the different types of constitution that are responsible for present-day dermatologic entities.

I feel gratified at this addition to the knowledge of this condition; whereas these patients are malnourished and present signs pointing to tuberculosis, I think that one can definitely take the disorder out of the category of tuberculosis per se.

Dr. William Allen Pusey, Chicago: I am glad to hear this paper and am interested in the findings. It has seemed to me from the start that the factor in acne conglobata is nonspecific. I think that if the Latin term were replaced by the name "globular acne," one could perhaps get rid of some of the confusion. As I follow the paper, the significant facts are these: The patients are cachectic persons with large sebaceous glands and many comedones. They have the disorder for a long time. One can produce the lesions with practically any pus-forming organism in persons with this sort of skin. I think that much loose thinking will be avoided if one says simply that the disease is an acne that has run wild in a cachectic subject.

Dr. Bedford Shelmire, Dallas, Texas: I do not think that we should consider acne conglobata as one of the varied types of acne, as suggested by

Dr. Pusey. The etiologic agents in the two conditions may be the same, but the clinical picture is entirely different. I have presented on various occasions before the Texas Dermatological Association a young man, aged 27, with a most extensive acne conglobata. As the eruption began before he was 2 years of age, the time element alone should exclude the entity from the acne group.

Dr. Walter J. Highman, New York: In nomenclature acne conglobata is simply a name, as Dr. Pusey suggests. In reality it is a suppuration in a person with acne who has a peculiar predisposition. That it occurs in cachectic persons I think is due to the fact that an enormous surface of the skin is affected and the cachexia is the result, not the cause, of the acne. I have watched two or three cases and have seen the disease develop in children with acne. As it persisted for years the children became cachectic. A patient treated in Boston subsequently came under my observation. He was cured through the simple procedure of evacuating pus and resecting areas of the skin that were riddled with lesions. I thought at the time that the conclusions that Dr. Belote has given were correct, namely, that the disease occurs in a particular type of person and that of many persons afflicted with acne only a few present this picture. The condition never seemed to me to have any relation to tuberculosis, except in the way Dr. Weidman brought out, and I think that Dr. Belote has substantiated that view.

Dr. William Allen Pusey, Chicago: Many of my cases demonstrated Dr. Highman's suggestions. In one boy the disease cleared up beautifully under roentgenotherapy, and the lesions evacuated themselves easily. This patient had a great many lesions, owing to long-continued acne. I think that the point Dr. Highman made is good, that the cachexia may be due to the pyemic infection.

Dr. Udo J. Wile, Ann Arbor, Mich.: I had the opportunity of studying these two cases with Dr. Belote from time to time, and also a third case.

As Dr. Pusey pointed out, it is well to simplify the classification of diseases, but I cannot subscribe to the statement that this is an acne running wild. I think that it is due to some other process. I cannot conceive of such a disease affecting the knuckles, backs of the hands and remote parts of the body where sebaceous glands are rare. I think that Dr. Highman's interpretation is rather better. I think that the subject might be simplified if the disease described as dermatitis nodularis necrotica could be included in this group. I believe that these cases are not essentially different, except in the fact that in dermatitis nodularis one does not have comedone formation. The two diseases are otherwise counterparts. The lesions occur in large areas and in ill nourished, cachectic persons. The patients that I have had were of low mental status. I think it unfortunate that the name acne has been attached to this disorder, but it might be a great mistake to label it something else at this time and further confuse the picture.

Dr. George M. MacKee, New York: It is probable that this infection can be placed in the pyodermia group. It is, I believe, the same disease that was formerly called acne cachecticorum. In a well developed case, one would not think of acne vulgaris, but there are borderline cases in which the differentiation between acne vulgaris and acne conglobata is difficult to make. Also, there are cases of acne vulgaris that may persist for a long time and then develop into the type that one must place in this category, showing the relationship between the two diseases and the fact that the patient has become less resistant to pyogenic organisms. It is common to find some defect in the patient, such as anemia, diabetes, foci of infection, etc., but in some cases it is impossible to demonstrate any particular reason for the lack of resistance. In such cases about the only conclusion is that the patient is in a certain allergic state or in a low state of specific resistance.

DR. WILLIAM H. MOOK, St. Louis: There seems to be a marked similarity in the clinical appearance of these cases. I had two patients in the same family in St. Louis who came from Mississippi. Both of them had had the disorder for many years, and another brother and sister at home were said to have it. The picture was almost identical with that in these cases. I rather thought that the cases belonged to the group of acne cachecticorum of unusually severe type.

DR. GEORGE H. BELOTE, Ann Arbor, Mich.: I am grateful to the members for their excellent discussion. It seemed to me that in an experimental report, such as this necessarily was, it was not proper for me to go into the classification and the relation to the other pyodermias. It seemed to me a little outside the scope of this particular paper.

The thing that aroused my interest at first was that even though Dr. Michelson doubted the specificity of the organisms, no other interpretation of his findings seemed possible; i. e., he was dealing with a specific organism. When I found that I was able to reproduce the disease in another patient with organisms of a different type, I began to be suspicious that it was perhaps not as specific as had formerly been thought.

SENSITIZATION AND DESENSITIZATION IN MAN WITH SNAKE VENOM (ANCISTRODON PISCIVORUS)

SAMUEL M. PECK, M.D.
NEW YORK

Experimentation on rabbits has shown that a small amount of moccasin venom given intradermally produces, after an incubation period, a refractory state to the experimental purpura, known as the Shwartzman phenomenon.[1] In an effort to discover whether snake venom could serve as a nonspecific method for raising the resistance of vessels to hemorrhage, an attempt was made to treat diseases such as thrombocytopenic purpura, hemophilia, familial hemorrhagic tendencies and functional uterine bleeding with this substance. In addition, various allergic diseases, such as hay fever and urticaria, were also treated. A preliminary report on the clinical results obtained has been published.[2] This report deals with the development of cutaneous sensitivity following repeated injections of the venom in a group of allergic patients and in a group treated for hemorrhagic tendencies.

METHOD OF ADMINISTRATION

The venom used was that of the moccasin snake (Ancistrodon piscivorus). It was obtained through the courtesy of the Antivenin Institute, H. K. Mulford Laboratories. A 1:3,000 dilution in physiologic solution of sodium chloride was used. The injections were given intradermally. Two tenths of a cubic centimeter of this dilution was given at the first injection, and it was usual to give subsequent injections of 0.4 cc. twice a week. The first five or six times care was taken that the sites of injection were separated by at least 10 cm.

REACTIONS TO INJECTIONS OF VENOM

Usual Reactions.—Intradermal injections of from 0.2 to 0.4 cc. of the 1:3,000 dilution of venom formed a wheal with some surrounding redness. The wheal usually increased in size to 1 or 2 cm., and the area of redness became more intense and extended for several centimeters around the wheal. The maximum reaction was reached in one-half hour, and then it began to subside. In a number of persons an area of ecchymosis was formed at the site in from three to twenty-four hours and in rare cases after one hour. The tendency to form ecchymoses after an injection of this concentration of venom varied a great deal

From the Division of Laboratories of the Mount Sinai Hospital.

1. Peck, S. M., and Sobotka, H.: J. Exper. Med. **54**:407, 1931.
2. Peck, S. M.: Proc. Soc. Exper. Biol. & Med. **29**:579, 1932.

with the individual. However, in patients with hemorrhagic diathesis, especially those having purpuric manifestations, it was almost the rule for the ecchymoses to form. The ecchymotic areas varied from 1 or 2 cm. to as much as 5 cm. in diameter. It was rare to have any hemorrhagic reaction in a normal individual or in those constituting the allergic group. After a number of injections of snake venom the tendency to form ecchymoses disappeared. Concomitant with this lessened tendency to hemorrhagic reactions, there were formed in the blood of both human beings and animals antihemorrhagins against the snake venom. A more detailed report of these findings will be given in another paper. No necrosis has been seen in any of the cases in which venom in this concentration was used.

Reaction of Hypersensitivity.—The reaction of hypersensitivity usually appeared after the fourth or the fifth injection, about fourteen days after treatment was begun. It was characterized by the formation of an egg-shaped swelling, which was hot, red and tender. The swelling varied from a few centimeters to as much as 10 cm. in diameter in very sensitive persons. It appeared in from three to ten hours after the injection, and reached its maximum intensity in from twelve to twenty-four hours. The swelling persisted for from twenty-four to ninety-six hours and then gradually subsided. In some persons a bluish discolored skin was left and in others an area of subcutaneous induration several centimeters in diameter was felt after the reaction had subsided.

As a rule there was no generalized reaction. In several of the patients there was a moderate rise in temperature at the height of the swelling. A marked reaction developed after the fifth injection in one of the patients, twenty-eight days after the first dose. The swelling began to develop four hours after injection, and remained as a large, swollen, tender area for four days. Concomitant with the development of this swelling, all the other sites of previous injections flared up, and small, indurated, erythematous areas developed.

The shortest period in which a changed reaction appeared was after the second injection, namely, six days after the beginning of the treatment. The longest period was that which elapsed after the fourth injection, or ninety days after the beginning of treatment. However, the fourth injection was given after a lapse of seventy days, because the patient did not return for further observation before this time. It is probable that in this case a reaction of hypersensitivity could have been elicited much sooner.

The immediate reactions to the intradermal injections of venom, even in hypersensitive persons, were negative.

Desensitization.—Desensitization was successful in fifteen of the sixteen cases in which it was attempted. The quickest method was to

continue with small doses of the 1 : 3,000 dilution, beginning with 0.02 cc. and increasing to 0.4 cc. by the fourth or fifth injection. The injections were given twice weekly, and usually desensitization was successful by the fifth injection. When the first few cases of sensitivity developed, high dilutions were used for subsequent injections in order to avoid severe swellings. It was observed, however, that it took much longer to desensitize by this method than by the previous one. In order to avoid unpleasant local reactions in attempting desensitization, it has been found that injections of the following doses are satisfactory: 0.1 cc. of 1 : 10,000; 0.4 cc. of 1 : 10,000; 0.2 cc. of 1 : 6,000; 0.4 cc. of 1 : 6,000; 0.1 cc. of 1 : 3,000, and 0.4 cc. of 1 : 3,000. Injections were continued even though some of the doses caused a local reaction.

In one case it was impossible to obtain densitization. This patient had urticaria and became sensitive following the second injection, eight days after treatment was commenced. There was marked swelling after the injection of 0.1 cc. of 1 : 60,000 dilution. The reactions to even high dilutions were so severe that further attempts at desensitization were abandoned.

Passive Transfer.—Passive transfer of the hypersensitivity according to the method of Prausnitz-Küstner was attempted with the serum of four hypersensitive patients. Blood was taken from the patients a few days after the reaction of hypersensitivity had developed. A subsequent injection showed that hypersensitivity was still present. Passive transfer was successful in only one patient.

COMMENT

Hypersensitivity developed in 75 per cent of the patients who were allergic and in 50 per cent of the patients in the hemorrhagic group following repeated injections of snake venom. A number of the patients had been tested by the scratch and by the intradermal methods for hypersensitivity to pollens, proteins, tuberculin and trichophytin previous to the injections of snake venom. There was no effect on the degree of the reactions to any of these substances in persons having positive reactions, even after the venom had been given for a long time. While a number of the patients with urticaria seemed benefited by the treatment with snake venom, the clinical results as a whole were not satisfactory. These results were in contradistinction to those in patients having bleeding symptoms in whom the clinical effects were very encouraging.

Zozaya and Stadelman [3] reported a positive passive transfer from a patient sensitive to crotalus, who manifested a hay fever type of reaction on handling the dried venom. The scratch test showed an immediate positive reaction in this patient.

3. Zozaya, J., and Stadelman, E. F.: Bull. Antivenin Inst. America **3**:93, 1930.

SUMMARY

Hypersensitivity to moccasin venom developed in 75 per cent of the patients with allergic manifestations after a number of intradermal injections. A changed reaction also developed in 50 per cent of non-allergic patients treated in the same manner. It usually required four or five injections, about fourteen days, for hypersensitivity to develop, although both the number of injections and the time required to produce hypersensitivity varied a great deal. Desensitization was possible in fifteen of the sixteen cases in which it was attempted.

Specific reagents in the blood of hypersensitive persons could be demonstrated in only one of four cases in which passive transfer was attempted.

URINARY PROTEOSE IN DERMATOSES

F. J. EICHENLAUB, M.D.
WASHINGTON, D. C.

Barber and Oriel have called attention in three articles to their investigations on urinary proteose in dermatoses. Their article in the *Lancet*, written in 1930,[1b] contains detailed information on the application of this work to dermatology.

In this article, the following essential information is brought out:

If the urine from cases of allergic and febrile diseases is acidified with sulphuric acid and shaken with a fifth of its volume of ether, the ethereal layer formed on standing, instead of being for the most part clear, as in normal people, becomes opaque, and has a waxy appearance. In strongly positive cases we noted that the tube could be inverted without spilling the contents.

The method of preparing the proteose is described as follows:

A twenty-four hour specimen of urine is collected from a case showing active symptoms, and put in a Winchester bottle containing a little chloroform. Approximately 400 cc. is placed in a separating funnel, rendered acid to Congo red with sulphuric acid, and shaken with 100 cc. or less of ether. Should the specimen contain urates, it is rendered alkaline with dilute caustic soda to dissolve them, and subsequently made acid. When the two layers are separated, the ethereal layer is treated with an equal volume of alcohol, and the precipitate allowed to settle. The latter is then collected by centrifuging in a sterile centrifuge tube. This tube is then inverted in an incubator at 37 C., and the alcohol and ether, present in the precipitate, are allowed to evaporate. When dry, the precipitate is dissolved in sterile N/10 sodium hydrate. The quantity of sodium hydrate required varies with the case, but 2 or 3 cc. are usually sufficient. Taking the usual aseptic precautions, 1 cc. of this solution is added to 9 cc. of 0.5 per cent phenol dissolved in normal saline. We are accustomed to call this dilution 1 in 100 for convenience. The quantity of precipitate obtained is usually about 0.3 Gm., so that the NaOH solution is approximately 1 in 10, but, as weighing each precipitate would involve loss of sterility, the exact quantities are ignored. Further dilutions of 1:1,000, 1:10,000, 1:100,000 and 1:1,000,000 are made. The sterility of the solution is then tested by inoculating an agar slope, and incubating for 48 hours. If care is taken, the solutions are usually sterile.

The chloroform in the 24 hour specimen and the subsequent treatment with ether and alcohol, seem to kill the contaminating organisms. This is fortunate, as heating destroys some of the properties presently to be described.

Read at the Fifty-Fifth Annual Meeting of the American Dermatological Association, Havana, Cuba, May 3, 1932

1. (*a*) Barber, H. W., and Oriel, G. H.: Lancet **2**:1009, 1064, 1928. (*b*) Oriel, G. H., and Barber, H. W.: ibid. **2**:231, 1930; (*c*) Compt. rend. VIII Cong. internat. de dermat. et syph., 1930, p. 497.

This is followed by a discussion of the chemistry of the proteose. Those interested are referred to the original article.

Barber obtained the proteose from a patient with serum sickness, and injected it intradermally at two sites (*a* and *b*). Twenty-four hours later, 0.025 cc. of a 1:100,000 dilution of proteose was injected intradermally into site *a*, and a control injection was made into another site (*c*). Into site *b*, 0.025 cc. of the same dilution of proteose from a patient with prurigo was injected. The injection into site *a* produced a strongly positive reaction; those into sites *b* and *c*, negative ones. This was essentially a positive Prausnitz-Kustner reaction.

Another test of the specificity of the substance was the following:

> Two areas of skin of a normal person were injected with the serum of a patient in a state of allergy towards horse serum; as is well known, the antibodies contained in the sensitized serum are fixed by the skin at the site of injection so that when, 24 hours later, the specific antigen is injected at the same site, an urticarial wheal results. Of the two areas thus sensitized, the one (*a*) developed a characteristic wheal of considerable size, with a temporary flare and lasting many hours, after injection of the patient's proteose in high dilution, whereas the other (*b*) gave no response to the proteose of another patient; the nonsensitized area (*c*) did not react to the proteose of the case of serum sickness, which was also injected into another normal subject without response.
>
> Intradermal injections in a dilution of 1:100,000 of the proteose obtained from this case of serum sickness were then made in three subjects known to be horse-sensitive, and positive reactions were obtained. Proteose in the same dilution from an allergic patient, non-sensitive to horse, gave negative reactions. In one of these patients—a horse asthmatic—the intradermal injection of the proteose from the patient with serum sickness was followed by rhinorrhoea and slight asthma the same evening although he had not had these symptoms for some time previously.

From these experiments, Barber and Oriel conclude that the proteose contains the specific antigen in allergic cases. They quote the works of Manwaring,[2] and conclude that:

> In some allergic states the substance responsible for the symptoms, partially, at any rate, is a product of tissue damage, resulting from the action of primary antigens on sensitized cells, particularly those of the liver, and acting as a secondary antigen.

The authors reported the results obtained in dermatologic conditions such as urticaria, angioneurotic edema, prurigo simplex, prurigo of Besnier (neurodermatis), dermatitis herpetiformis, psoriasis and sensitization to light of the adult type. Sixteen of nineteen patients who had urticaria were well at the time the report was made. Thirteen patients with simple prurigo were so treated with good results in nine

---

2. Manwaring, W. H.; Hosepian, V. M.; O'Neill, F. I., and Moy, H. B.: J. Immunol. **10**:575, 1925. Manwaring, W. H.; Reeves, D. L.; Moy, H. B.; Shumaker, P. W., and Wright, R. W.: J. Immunol. **13**:63, 1927. Manwaring; Marino, D. H.; McCleave, T. C., and Boone, T. H.: ibid. **13**:357, 1927.

cases. Five of fourteen patients who had prurigo of Besnier were free from symptoms, and the rest were improving. Of nine patients with dermatitis herpetiformis who were so treated, four were free from symptoms. The results obtained with this treatment in psoriasis (number of cases not stated) were not very satisfactory.

In my own work, I have found that the presence of the "ether reaction" is of little value. Many apparently normal persons give such a positive reaction. Indeed, the test was used by Closcz [3] in 1890 as a delicate test for the presence of protein in urine. However, the test should be performed for each specimen of urine before an attempt to extract the proteose is made, as some specimens of urine have been found to be entirely negative.

I have been able to confirm two of Barber and Oriels' observations on the specificity of the antigen in the proteose. Three of our patients who gave positive reactions to their own proteose were tested with the proteose obtained from the others. In no case was there a reaction to any but the patient's own proteose. In performing these tests, the same dilutions that caused reactions in the patient were used in the subjects with an indifferent response.

The Prausnitz-Kustner reaction was also confirmed. The patient in case 6, who had a neurodermatitis of the elbows, reacted to a 1:1,000 dilution with an erythema measuring 1 inch (2.54 cm.) by three-fourths inch (1.9 cm.) after twenty-four hours. Blood serum from this patient was injected intradermally into my forearm. Twenty-four hours later, 0.05 cc. of this patient's proteose was injected into this area, and a similar amount about 1 inch away. Both of these areas showed a pronounced erythema, the one in the center being about 1 inch in diameter and the one at the edge, one-half inch, so that they merged. A definite palpable edema was present. This reaction took three days to subside. Evidently the injection meant as a control was too near the site where the serum was injected, as another injection of an equal amount into the opposite forearm caused only a small transient erythema which faded in eight hours, and disappeared the next day.

I have made a few minor modifications of the procedure of treatment. Epidermal or scratch tests were of little value in my cases. An injection of 0.05 cc. of each dilution is given intradermally, only one solution being used at each test, until the dilution causing a reaction is determined. After that, gradually increasing doses of this solution are given, and stronger solutions are administered as the local and general reactions dictate. In general, better results have been secured with biweekly injections, although this method cannot be used for highly sensitive patients. When the patient reacts to solutions of 1:1,000,000

3. Closcz, quoted by Kahresier: Thierärztl. Chem. **20**:215, 1890.

or 1 : 100,000, the dose must be increased very slowly, as severe general reactions may be caused, as in case 2. In such cases, the antigen may be very active, and due caution must be observed.

In all dilutions 0.1 cc. and 0.2 cc. are given intradermally and larger amounts subcutaneously.

Instead of phenol, cresol, U. S. P., is used as a preservative, as it is less irritating to the tissues. The solutions are put up in vaccine bottles for easy administration without destroying the sterility.

REPORT OF CASES

CASE 1.—O. F., a white man, aged 39, a grocer, presented a patchy, bright red, scaly and vesicular dermatitis on the face, hands and arms. The condition was probably occupational, but the article or articles producing it could not be determined.

The patient had two brothers who were also grocers. Each of them had been treated for occupational eczema of the hands. In each, the condition cleared up promptly with appropriate local treatment.

In the patient, however, the condition resisted all the usual methods of local and general treatment, including roentgen and ultraviolet irradiations, which were given from Feb. 25 to July 5, 1931. At this time a proteose solution was secured from his urine. On July 5, 0.1 cc. of a 1 : 10,000 solution produced a slight reaction. On July 12, the intradermal injection of 0.15 cc. of the same dilution was followed by a distinct, red, itchy, papule 5 mm. in diameter, which was still present, but fading on July 20. On this date, 0.1 cc. of a 1 : 10,000 dilution was again given intradermally. On July 28, there was only a slight reaction at the site of the last injection, but the papule caused by the injection given on July 12 had become larger and redder; subsequently it ulcerated at the top and healed in about three weeks, leaving a distinct, round, depressed scar. This lesion in many respects resembled a tuberculid. Treatment was continued with gradually increasing doses until Oct. 5, 1931, with no other medication. At that time, the eruption was practically well and subsequently healed completely, with no relapse to the date of writing.

CASE 2.—M. H., a white girl, aged 11, when first seen in 1924, had a vesicular dermatitis of the hands and feet, with occasional patches on the arms and legs, which had recurred from time to time since she was 1 year old. The family history was negative for allergy. The patient had a mild type of hay fever at times. In 1924, she responded well to the usual treatment plus roentgen therapy and ultraviolet irradiation. Similar results were obtained in 1926, 1927 and 1931. In 1931, however, the patient failed to respond to treatment as before, and further roentgen treatment was contraindicated.

The patient showed a slight reaction to the injection of 0.1 cc. of a 1 : 10,000 dilution of her proteose. She was treated with gradually increased doses until Feb. 15, 1932, when the eczema had disappeared. No other treatment was used.

CASE 3.—C. C., a white man, aged 45, had vesicular eczema of the backs of the hands and, occasionally, of the feet which had recurred from time to time for eight years. It always responded to roentgen therapy, but a relapse occurred promptly, so that further roentgen treatment had to be given with caution.

On Aug. 3, 1931, treatment with proteose was started. On the injection of 0.1 cc. of a 1 : 10,000 solution, a definite papule developed, which had almost faded at the end of a week, when 0.15 cc. of a 1 : 10,000 solution was given. This injec-

tion caused a mild local reaction and also a general reaction consisting of fever, malaise and headache, following which the papule at the site of the first injection became enlarged and ulcerated in the center; it healed in about three weeks, with scar formation. This lesion also resembled a papulonecrotic tuberculid. It was never possible to increase the dose above 0.1 cc. of a 1:10,000 dilution without causing the aforementioned general reaction. With the patient under continued treatment with this dosage, the eczema disappeared, without other treatment. However, treatment was irregular, and relapses have occurred. Whether or not the patient will subsequently be cured cannot be said at present, but he has been definitely benefited by these injections.

Case 4.—E. M. D., a white man, aged 30, had chronic recurring urticaria of four months' duration. He had failed to respond to any previous treatment for this condition. Until the time of writing, no definite local or general reaction has been obtained to injections of proteose given in dilutions up to 1:1,000. Relief from hives has been obtained, but as this has occurred before I am unable to say whether or not the treatment is responsible.

Case 5.—W. J., a man, aged 60, had a chronic generalized, scaly eczema. No positive reaction was obtained with injections of proteose, and treatment with dilutions up to 1:1,000 failed to be of benefit.

Case 6.—E. M. E., a white woman, aged 38, had neurodermatitis of both forearms below the elbows, of one year's duration. She had a positive reaction to a 1:1,000 solution of proteose, with a definite erythema with palpable edema which persisted for forty-eight hours. She received eight injections and is well. However, she was also given a few roentgen ray treatments, which probably caused the disappearance of the lesion. Proteose is being used largely to prevent a relapse, which so commonly occurs in these cases.

Case 7.—B. F., a white man, aged 20, had generalized itching due to chronic subacute urticaria of five years' duration. All previous treatment had been unavailing. The injection of 0.2 cc. of a 1:100,000 dilution of proteose caused a definite, local reaction which persisted for forty-eight hours. He was treated once a week from Dec. 1, 1931, to Feb. 24, 1932, when he was entirely free from symptoms. Subsequently he had a mild relapse, but responded to further treatment. No other type of treatment was used.

Case 8.—R. Q., a white girl, aged 8 years, who was first seen in October, 1928, whose family history was negative for allergy, each summer had severe asthma and hay fever due to ragweed. At the time she was seen she presented a red, scaly eczema in each antecubital fossa. This condition had been present off and on for three years; it had no relation to the ragweed season. The patient was treated several times between 1928 and 1931, with indifferent success.

On Dec. 14, 1931, injections of 0.1 cc. of the 1:1,000,000 dilution of her proteose caused a definite cutaneous reaction, 2 cm. in diameter, which persisted for forty-eight hours. Gradually increasing doses have been given once a week since then. The eczema had entirely disappeared by April 1, 1932.

Case 9.—H. B. H., a white man, aged 40, had a dermatitis, apparently of external origin, on the hands, arms and legs. He did not show a definite reaction to any dilution of proteose. Treatment with this solution in a dilution of 1:1,000 over a period of two months caused no improvement.

Case 10.—L. U., a white man, aged 20, had a severe, generalized psoriasis of ten months' duration. Nine roentgen and several ultraviolet treatments caused no improvement. Chrysarobin was also ineffective. The patient did not show a definite local or general reaction to the injection of proteose. He was treated

twice a week from Nov. 7, 1931, to Feb. 1, 1932. The psoriasis entirely disappeared. This patient also had painful joints in the hands and knees, probably a mild arthritis which is sometimes seen with psoriasis. This, too, disappeared as a result of treatment.

CASE 11.—B. S., a white girl, aged 12, whose family history was negative for allergy, had had eczema since infancy. When she was 2 years old, this condition disappeared. When she was 7, the eczema, together with asthma and hay fever, the latter due to ragweed, appeared simultaneously. The eczema had persisted constantly ever since, and the asthma and hay fever recurred in a severe form each fall. Attempts to desensitize with pollen caused an allergic reaction which almost killed the patient.

In September, 1931, treatment with proteose was started; 0.5 cc. of a 1:1,000,000 solution caused a transient local reaction and a slight aggravation of asthma. This was repeated without trouble. On the third injection, the dose was stepped up to 0.15 cc. of a 1:1,000,000 solution. This caused a severe flare-up of the asthma, which caused the patient to go to bed for a week. Subsequently, no further increase was made in the dose. By November 11, the eczema had disappeared. The asthma had also disappeared, but, of course, the pollen season was over. The patient, however, was well for the first time in five years.

CASE 12.—M. C., a white woman, 30 years of age, when first seen in September, 1924, had an older sister with a cutaneous condition of an almost identical appearance; otherwise, the family history was irrelevant. The patient presented marked xeroderma and red, scaly eczema of the face, the front of the arms and the neck of the type of a neurodermite. In 1924, the basal metabolism was —13. With thyroid medication and roentgen therapy, the eczema cleared up, and the general condition improved. In December, 1931, the patient returned with a recurrence of the condition. The injections of 0.05 cc. of a 1:1,000,000 and of a 1:100,000 dilution of proteose produced mildly positive reactions. The patient was treated until Jan. 13, 1932, with considerable improvement. She then failed to return, and the subsequent result is unknown.

CASE 13.—Mrs. P. F., aged 66, had a severe case of psoriasis. In the first attack, for which treatment was begun on March 12, 1931, the patient responded to roentgen therapy. In October, 1931, after a relapse with failure to respond to roentgen irradiation or other treatment, injections of proteose were started. The patient had no marked local reaction. She was treated twice a week with rapidly increased doses, and by December the condition had almost entirely cleared up. However, a relapse occurred promptly in January, and subsequent injections did not have much effect.

CASE 14.—V. K., a white girl, aged 13, whose history was negative for allergy, presented generalized, scaly eczema on a xerodermatous skin. She showed a slight reaction to the injection of a 1:100,000 solution of proteose. Treatment given from September until December, 1931, caused a practically complete disappearance of the eczema. In January, a relapse occurred. After the sixth injection of proteose in the second course of treatment, the eczema improved, but marked urticaria developed, which subsided when the administration of proteose was stopped. Further treatments with proteose could not be given because of this reaction.

CASE 15.—W. E. M., a white man, aged 40, who was first seen in 1927, had eczema of the ear and leg. The family history was negative for allergy. The patient always responded well to roentgen therapy, but in 1931, further treatment of this type was contraindicated.

A definite red papule, which persisted almost a week, appeared at the site where the 1:10,000 dilution of proteose was injected. The patient has been

benefited by treatment, but he has not appeared regularly for treatment, and no conclusions can be drawn.

CASE 16.—H. G., a white girl, aged 16, had had a severe generalized, scaly and vesicular eczema since infancy. A brother had a severe case of asthma; otherwise the family history was irrelevant. The patient had not responded to any type of treatment. The use of roentgen and ultraviolet irradiations, a restricted diet, arsenic and topical applications had failed. Injections of proteose caused neither a local nor a generalized reaction. Treatment over a period of six months had no effect on the eruption.

CASE 17.—S. N., a white girl, aged 14, had had generalized severe eczema since infancy. All types of treatment failed to affect the eruption materially. The patient did not have a local or a general reaction to proteose, and injections of this substance have failed to affect the eruption.

CASE 18.—M. M., aged 38, a white man, had severe generalized dermatitis herpetiformis of ten years' duration. The patient stated that he had not had a full night's sleep since the onset of the condition because of the severe itching. When he was first seen, he was covered from head to foot with groups of small papulovesicles and crusts. He had received roentgen and ultraviolet irradition, autohemotherapy, arsenic and other types of treatment without avail. Reactions consisting of a wheal-like papule and erythema which lasted over forty-eight hours were produced by the injections of 1:100,000 and 1:10,000 dilutions of proteose. After three weeks of biweekly injections, the itching subsided and the eruption was 90 per cent better. Further treatment was given in his home town. Three months later, after treatment was discontinued, the patient had a mild relapse; again he responded to treatment with proteose. His physician wrote to me that in December, 1931, four months after treatment was started, only pigmentation remained.

CASE 19.—A white woman, aged about 35, had lobar pneumonia. The family history was negative for allergy. The patient had never had eczema, hay fever, asthma or any other allergic disease. Her proteose, obtained while the pneumonia was active, caused a marked local erythema and a wheal when injected in a dilution of 1:1,000,000. This patient was tested to determine whether or not reactions were present in frank infection as well as in allergic conditions.

ANALYSIS OF THERAPEUTIC RESULTS

The patients in the eighteen cases herein recorded have been observed sufficiently long to justify some observations. No definite conclusions as to the value of the method can be attempted in such a short experience. Furthermore, the nature of the foregoing cases is such that spontaneous improvement may be easily attributed to the treatment. Of course, the end-results are uncertain after such a short period of observation.

Five patients with localized types of eczema usually associated with external irritation were treated. In one case, treatment was a complete failure; in three improvement occurred, and in one cure has been obtained to the time of writing.

Six patients who had generalized eczema of the type usually associated with constitutional allergy, that is, cases of long duration and

often accompanied by asthma, hay fever, a family history of allergy and a xerodermatous type of skin, were treated. In three cases, the treatment was a complete failure. Three patients were markedly improved.

Two patients with psoriasis received treatment. In one, the condition cleared up entirely; in the other, temporarily, with a subsequent relapse.

A patient with neurodermatitis was improved, but the result may be due entirely to roentgen treatment.

A patient with generalized eczema was improved, but urticaria developed from the injections.

A patient with dermatitis herpetiformis was markedly improved; in this case, all other types of treatment had proved ineffective.

Two patients with chronic urticaria were treated. One was very much improved. In the other, the result is still in doubt.

In a case of pneumonia in which there was no personal or family history of allergy the reaction to a 1:1,000,000 dilution of proteose was strongly positive. The patient was tested to determine whether or not positive reactions may occur in cases of frank infection.

It is only fair to note that in cases in which complete failure resulted, neither local nor general reactions were obtained. It is possible that in these cases the urine was obtained at a time when no antigen was present in the proteose. On the other hand, in a case of psoriasis the patient responded to treatment even though no local reaction occurred. In general, however, treatment should be used in only those cases in which a reaction is produced by intradermal injections.

All of the patients who gave definitely positive cutaneous reactions, that is, ten of the eighteen patients with dermatologic conditions, appeared to receive some benefit from treatment. Only one of the other eight patients improved.

It should be noted that in two cases the papule caused by the first injection subsided and then flared up within twenty-four hours after the second injection, causing a necrotic papule which healed, with scar formation. The reaction looked not unlike that seen in papulonecrotic tuberculid. This again raises the question of the possibility of local allergic reactions causing the papulonecrotic type of lesions due to toxins alone.

Except in two cases the patients were treated only with proteose. It is probable that better therapeutic results can be obtained by combining these injections with general measures, such as diet, and with local applications, roentgen therapy and other treatment when indicated. When this is done, treatment with proteose will probably prove an added aid in the management of this type of case. Thus, in case 13 the patient with psoriasis responded very well to roentgen therapy after the injection of proteose, whereas previously she had not benefited by such treatment.

Since a positive reaction is obtained in a frank infection such as pneumonia, as well as in allergic conditions, it seems probable that the mechanisms of immunity and allergy are similar so far as the production of an antigen in urinary proteose is concerned. It is generally assumed that in infection the tissues have a locally lowered resistance. It is possible, therefore, that this may confirm the opinion of Pusey [4] and others that in eczema the skin has a lowered resistance to irritation.

CONCLUSIONS

1. The work of Barber and Oriel with urinary proteose is reviewed in some detail.

2. The method of preparing the proteose is comparatively simple, and it should be widely used definitely to determine its value.

3. It has been possible to confirm the specificity of the antigen by: (1) securing negative reactions to foreign proteose in patients who definitely reacted to their own proteose, and (2) obtaining a positive Prausnitz-Kustner reaction in a normal person.

4. Therapeutic results have been sufficiently encouraging to warrant further trial. They have not been definite enough to confirm entirely the value of this procedure.

5. The proteose is highly active in some persons. The patient's sensitivity to each of the dilutions should be carefully determined before treatment is started.

DISCUSSION

DR. GEORGE M. MACKEE, New York: Dr. Eichenlaub has presented facts which indicate that the specific substances to which the patient is sensitized are found in the urinary proteoses. His cutaneous tests and therapeutic results and those mentioned in the literature are interesting and encouraging, but they are not conclusive. As Dr. Eichenlaub said, much more work will have to be done before the method can be evaluated. Some of the work points toward real specificity, but his experience with psoriasis suggests the results with nonspecific protein therapy, such as have been obtained with various proteins and injections of whole blood. I should like to know the amount of proteose that Dr. Eichenlaub injects intradermally.

DR. WILLIAM H. GUY, Pittsburgh: This is a fascinating subject to me because of the large number of failures we have had in determining the substance to which patients were hypersusceptible. I remember in Dr. MacKee's office we carried out a great many tests, with almost a complete absence of reactions, until we got a definite reaction to pork in an orthodox Russian Jew. I think that experience has made me somewhat skeptical. Now we are dealing with the proteose that is secreted by the patients themselves and which is present in abnormal conditions and absent in normal persons. A large number of therapeutic failures in the administration of proteins or of protein substances have been due to the fact that one

4. Pusey, W. A.: Compt. rend. VIII Cong. internat. de dermat. et syph., 1930, p. 126.

was dealing not with split protein but with whole protein. Theoretically, from the standpoint of the use of the urinary proteose, there should be some hope in the situation.

Dr. H. J. Templeton, Oakland, Calif.: If this method is found of value, it will solve a great many problems in allergy. Instead of having to hunt for the primary allergen with patch tests, intradermal tests and elimination diets, all one would have to do would be to isolate the secondary allergen, the proteose, from the urine. I have treated about fifteen patients with urinary proteoses, and the results have not been satisfactory. However, I have to criticize my technic in that I have used relatively large doses. I have been desensitizing patients with a 1:1,000 dilution of proteose, but I think that Dr. Eichenlaub is correct in using higher dilutions. Moreover, I have treated only patients with cases of eczema who had previously been treated with practically all other methods with failure.

Dr. Fred Wise, New York: Dr. Eichenlaub is to be commended for work that represents a great deal of hard labor; however, I wish to call attention to one feature. For example, he said that one patient with neurodermite showed improvement, but that this improvement might have been due to roentgenotherapy. In experimental work of this kind, one must make up one's mind to limit oneself absolutely to one method in order to find out with what one is dealing.

Dr. F. J. Eichenlaub, Washington, D. C.: I am not sure whether the results obtained by this treatment are due to a nonspecific reaction or to a specific one. The tests for specificity are outlined in the body of the paper, and seem fairly conclusive. With one exception, every patient so treated had received months of other types of treatment, including, in some cases, injections of nonspecific protein without result. Proteose has been used only in those cases in which other types of treatment have failed.

Perhaps my explanation of the method of testing a patient was not sufficiently clear. At first, 0.05 cc. of a 1:1,000,000 dilution is given intradermally, and if no reaction occurs a test with a 1:100,000 solution is made after twenty-four hours. The reason for doing this is that if a test is made with too large a dose at one time in a patient who is oversensitive, he may become extremely ill, as did two patients whose cases I reported.

Regarding Dr. Wise's criticism, only two patients were treated by any other method during my work. I am not overly enthusiastic, but I think that the procedure should be given a reasonable trial to see whether it is of value.

News and Comment

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

The organization of the American Board of Dermatology and Syphilology has been completed and the Board is now prepared to receive applications for certificates.

During the first two years following the incorporation of the Board certificates may be issued without examination to certain dermatologists and syphilologists of high professional attainment and prestige. For the present it is requested that application be restricted to those who have limited their practice to dermatology and syphilology for the past fifteen years or more or to those of professorial rank in class A medical schools. All who desire to receive a certificate from the Board must fill out an application blank and comply with certain other requirements.

Examinations for other groups will be held in the fall of 1933. Due notice of the time and place of such examinations will be published in this journal at a later date.

Application blanks and booklets of information may be obtained from the secretary, Dr. C. Guy Lane, 416 Marlboro Street, Boston.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

A CLINICAL STUDY OF ARTIFICIAL HYPERTHERMIA INDUCED BY HIGH FREQUENCY CURRENTS. F. W. BISHOP, C. B. HORTON, S. L. WARREN and E. LEHMAN, Am. J. M. Sc. **184**:515 (Oct.) 1932.

In the series of fifty-seven cases reported, eighteen were cases of syphilis of the central nervous system and fifteen of chronic arthritis, the remainder being instances of various types of infection. The apparatus used was a special octagonal box that completely covered the patient and more easily controlled the temperature. The authors considered it safe to keep the temperature at any desired level below 42 C. for five hours for the average patient. With a few exceptions, patients with dementia paralytica showed great clinical and psychic improvement, the chemical changes resembling those observed after malarial therapy. Patients to receive this treatment should be carefully selected in order to avoid untoward results.

CONTACT DERMATITIS (VENENATA). DISTRIBUTION AND IMPORTANCE OF THE HELENIUMS AS A CAUSE OF CONTACT DERMATITIS IN THE UNITED STATES. R. M. BALYEAT, H. J. RINKEL and T. R. STEMEN, Am. J. M. Sc. **184**:547 (Oct.) 1932.

The plants of this family have been found to be the cause of many cases of dermatitis venenata throughout the Southwest. They are distributed over the whole of the United States, being fairly abundant and widely distributed in at least 50 per cent of the states.

The active substance is an oleoresin, nonvolatile and soluble in ethyl alcohol, benzene or ether. A 10 per cent solution gives the best results for patch testing; in some patients, however, systemic reactions of intestinal cramps, diarrhea, conjunctivitis and headache develop.

JAMIESON, Detroit.

OCULAR PEMPHIGUS. WILLIAM M. JAMES, Am. J. Ophth. **15**:815 (Sept.) 1932.

Two cases of typical ocular pemphigus are described; one of these occurred in a white man of unstated nationality and the other in a Negress. Eight months after the first patient presented himself he exhibited a generalized, gyrate, erythematomacular and plaquelike eruption with wheal-like disks and with large, tense bullae of the extremities. Lesions were also noted in the oral and pharyngeal mucosae. This eruption followed the ingestion of an amytal tablet and disappeared in three weeks without accompanying change in the ocular lesions. The second case showed only two vesicles of the umbilical region at the time of examination. Phytopharmacologic tests on the serum of both patients were positive. Biomicroscopic observations on these two patients showed the first changes to consist of perivascular thickening resembling fine striae, which on movement of the conjunctiva appeared to act as lines of traction. The superficial vascular network was enmeshed in fibrous tissue which produced contraction resulting in gross irregularities in the caliber of the vessels and later macroscopic scarring. Conjunctival formation of vesicles is thought by the author to be due to simple edema lifting the overlying epithelium which quickly exfoliates and is replaced by fibrosis rather than by new epithelium. Treatment of the ocular lesions was of no avail.

WIEDER, Milwaukee.

DIETARY PRACTICES IN RELATION TO THE INCIDENCE OF PELLAGRA: I. A STUDY OF FAMILY DIETARIES IN LEON COUNTY, FLORIDA. M. R. SANDELS and E. GRADY, Arch. Int. Med. **50**:362 (Sept.) 1932.

An examination of ninety-three dietary records from twenty-nine families of Leon County, Florida, showed significant differences in the use of milk and

succulent vegetables, with minor differences in the use of eggs, cheese and fruit. The records covered seven day periods and were collected from sixteen families with active cases of pellagra and from thirteen pellagra-free families. Seasonal variation in the supply of milk and succulent vegetables was also noted, and this influence was also more marked in the dietaries of pellagrous families.

JAMIESON, Detroit.

ERYSIPELAS IN THE NEW-BORN. FREDERIC W. TAYLOR, Arch. Pediat. **49**:587 (Sept.) 1932.

This is a report of a fatal case of erysipelas in a 2 weeks old infant girl. The onset was insidious; the condition was undiagnosed for three days. The first lesion noted was limited to the diaper area; other entirely distinct lesions of erysipelas appeared on other parts of the body. Hemolytic streptococcus and Staphylococcus albus were demonstrated in the subcutaneous tissues, and it is thought that the organisms, growing in symbiosis, caused the lesions described. The tissue sections indicated that the bacteria gained extrance through the hair follicles, and that the source of the organisms was probably from a low grade vaginitis. Erysipelas in the new-born and that in the adult are contrasted.

KERION CELSI. A. M. DAVIDSON and C. H. GREGORY, Canad. M. A. J. **27**:485 (Nov.) 1932.

Two cases of kerion occurring in brothers are reported. One of the patients had a lesion on the eyelid as well. Trichophyton album was recovered from both the scalp and the eyelid. Lichenoid trichophytids developed in both patients during the third week, following which the kerion and lesions of the eyelid disappeared. The appearance of the trichophytid is considered to have been associated with the development of a specific immunity which was responsible for the spontaneous cure.

RATTNER, Chicago.

XANTHOMA MULTIPLEX. WILLIAM P. FINNEY, HAMILTON MONTGOMERY and GORDON B. NEW, J. A. M. A. **99**:1071 (Sept. 24) 1932.

The authors report two cases of xanthoma multiplex associated with mild diabetes insipidus. In both cases lesions were present in the larynx and trachea, and in both there was a tendency for the cutaneous lesions to involve the flexor surfaces while sparing those parts exposed to trauma. There were no abnormal chemical changes in the blood, and there was no evidence of any disturbance of lipid metabolism. Treatment by means of diet, local roentgen exposures and injections of pituitary extract controlled the diabetes insipidus but had no effect on the xanthoma lesions.

THE ANTITOXIN TREATMENT OF ERYSIPELAS. DOUGLAS SYMMERS and KENNETH M. LEWIS, J. A. M. A. **99**:1082 (Sept. 24) 1932.

The authors report their results with the use of erysipelas antitoxin in 3,311 patients at Bellevue Hospital during the past five years. The routine treatment consisted of giving an early intramuscular injection of 10 cc. of the concentrated antitoxin to adults or children and repeating the injection from every twelve to twenty-four hours, depending on the severity of the disease.

In comparing this group of patients with 15,277 patients with erysipelas treated without antitoxin from 1904 to 1926, the use of antitoxin reduced the mortality from 10.1 to 7.1 per cent, and also reduced the duration of the disease about 60 per cent.

The antitoxin treatment of erysipelas is useful only in controlling the immediate attack, however, and does not render the patient immune to future attacks.

PRIMARY ACTINOMYCOSIS OF THE TONGUE. OLIN J. CAMERON, J. A. M. A. **99**:1146 (Oct. 1) 1932.

The author adds two cases of primary actinomycosis of the tongue to the fifty-three cases previously recorded, and states that the apparent rarity of the condition is due only to errors in diagnosis. He recommends surgical excision followed by local roentgen therapy and large doses of potassium iodide.

CARO, Chicago.

THE RÔLE OF SULFUR IN DERMATOLOGY. FRANK C. COMBES, New York State J. Med. **32**:1019 (Sept. 1) 1932.

The author presents a historical résumé of the use and abuse of sulphur, one of the oldest remedies. Precipitated sulphur and, especially, colloidal sulphur are of specific interest in dermatoses in which their value depends primarily on their ability to combine with keratin to form polyhydrogen sulphides and sulphurous acid. According to the author, the sulphur is absorbed through the skin when applied in a suitable medium and is absorbed by the gastro-intestinal tract when administered by mouth. It is of value in syphilis in stimulating the elimination of mercury and when given intramuscularly in the fever treatment of neurosyphilis.

FURTHER EXPERIENCES WITH TRICHOPHYTIN. LAIRD S. VAN DYCK, JEROME KINGSBURY, BINFORD THRONE and C. N. MYERS, New York State J. Med. **32**:1101 (Oct. 1) 1932.

The authors' further investigations on a second series of patients suffering with mycosis-like eruptions confirmed their earlier observations that a positive trichophytin test might be obtained in this group of patients. From these observations it appeared that the extract finds ready application from a differential diagnostic point of view. These observations were important in establishing the best mode of procedure in treating eruptions that sometimes closely simulate symptoms due to other causes. Analysis of the therapeutic results indicated that with a small number of treatments satisfactory clinical findings were obtained. Emphasis was placed on the importance of regularity in treatment, and also on the necessity of maintaining the concentration adequate to produce a local reaction. The average number of injections was twelve. A follow-up study of the first series of patients reported in 1931 showed that 93 per cent of those who returned were free from clinical symptoms; 26 per cent had had mild recurrences, which ultimately cleared up with additional treatment, and the patients were found among those cured. The average blood sugar for two hundred cases was 108 mg. per hundred cubic centimeters of blood, as compared to 90 mg. used as the authors' normal value (Hastings-McLean method). Various manifestations of sensitization to fungi are enumerated. The results of vaccinotherapeutics by subcutaneous injections of polymycotic vaccines were summarized from reports of other investigators. Mueller's explanation of intradermal therapy in general was discussed from the physiologic point of view. An attempt was made to explain the rationale of intradermal therapy as applied to mycotic infections of the skin, tuberculosis of the skin, sycosis vulgaris and occupational eczema.

THE VALUE OF AN EQUILIBRATED SALT DIET IN THE TREATMENT OF VARIOUS DERMATOSES: A MODIFICATION OF THE HERRMANNSDORFER-SAUERBRUCH-GERSON DIETS. JOSEPH JORDAN ELLER and CHARLES ROBERT REIN, New York State J. Med. **32**:1296 (Nov. 15) 1932.

A comparative review of the Gerson and the Herrmannsdorfer-Sauerbruch diets, together with a discussion of their advantages, disadvantages and difficulties of application, is presented. Chiefly because of the lack of palatability of the salt-free diets and the consequent difficulty to obtain the patient's full cooperation, Keining and Hopf developed a physiologically equilibrated salt mixture. Their

experiments determined that sodium was the harmful component of ordinary salt and that it could be rendered perfectly harmless to the organism by bringing it into definite proportional relationship with sodium-detoxicating cations, viz., potassium calcium and magnesium cations. Using this equilibrated salt mixture according to the directions of Keining and Hopf, twelve patients with dermatologic diseases were treated. Two of the patients had lupus vulgaris; two, lichen planus; four, chronic eczema of unknown etiology; two urticaria, and two, acne vulgaris. The patients with lichen planus and urticaria and two with eczema showed definite improvement. Two of those with eczema and the patients with lupus vulgaris and acne vulgaris were unaffected by the diet.

A Possible Etiology of Raynaud's Disease. Arthur F. Kraetzer, New York State J. Med. **32**:1304 (Nov. 15) 1932.

Five cases of Raynaud's disease are reported, two severe, one moderate and two abortive. Arsenic was found in all of them. Under treatment with sodium thiosulphate, not only did the symptoms of Raynaud's disease clear up, but associated symptoms theoretically producible by arsenic, such as pruritus, paresthesia and chronic fatigue, cleared up pari passu.

Alopecia Associated with Hypothyroidism in a Child. I. Newton Kugelmass, New York State J. Med. **32**:1371 (Dec. 1) 1932.

A case is reported in which the well recognized medical factors involved in the management of every case of generalized alopecia are emphasized. The author does not prove his case to be one of hypothyroidism or of endocrine imbalance, but he notes the return of hair following tonic treatment, a raw base-forming diet and the administration of thyroid and of solution of pituitary.

Traub, New York.

Viosterol in the Treatment of Pemphigus. John B. Ludy and C. M. Devalin, Urol. & Cutan. Rev. **36**:817 (Dec.) 1932.

The authors report six cases of pemphigus vulgaris in which the patients recovered following the oral administration of large doses of viosterol, varying from 12 to 45 cc. daily. They also refer to two other cases in which the patients recovered under the same treatment given by another physician. The diagnosis in all these was made on clinical grounds, and the Pels-Macht phytopharmacologic test was not applied.

In contrast to this group, they consider fifty-five cases of pemphigus seen previously in Philadelphia, in which the patients were treated without viosterol. Thirty-four of these patients were followed; thirty-three died, and the only patient who recovered was given an antipellagra diet and large doses of yeast.

Because of this response to therapy and the dietary history of their patients, the authors express the belief that deficiency in vitamins is an important factor in the etiology of pemphigus.

Caro, Chicago.

Hyperglycemia and Skin Diseases. Georg A. Rost, Brit. J. Dermat. **44**:57 (Feb.) 1932.

The previous reports on the relationship of hyperglycemia and diseases of the skin based on the oral test for dextrose tolerance of Baudoin are mentioned, and the disadvantages of this test are discussed. The present observations are based on a method worked out by Wislicki in His' clinic in Berlin, in which the dextrose is given by intravenous injection. The procedure is described and has been used by Rost in about one thousand cases. Tables (graphic) are shown to illustrate the results, and the author states that there are numerous reports in the literature based on a single value determined during fasting and a normal value of a different

height, describing hyperglycemia in several groups of diseases of the skin. The groups of conditions in which Rost made tests comprise nearly all those in which hyperglycemia has been found by others. He did not find pathoglycemic curves in acne, seborrheic eczema, furunculosis and other pyodermias, toxic dermatitis, dermatitis venenata, carcinoma or tuberculosis of the skin. He expresses the belief that in general there is no hyperglycemia in eczema, but that no doubt a small group of cases exists in which pathoglycemic curves are found. Pathoglycemic curves are often, but not always, found in intertriginous dermatitis and psoriasis. In neurodermatitis universalis ("flexural eczema"), he nearly always found a relatively low value during fasting, and there was a relatively great number of normally shaped curves. He believes that disorders of carbohydrate metabolism are occasionally connected with diseases of the skin. That certain groups of diseases of the skin are regularly connected with hyperglycemia is doubtful.

DEPOSITION OF GOLD IN THE SKIN. J. E. M. WIGLEY, Brit. J. Dermat. **44**:69 (Feb.) 1932.

An investigation was carried out to determine the presence of gold in the affected skin of three patients who had lupus erythematosus and in whom an eruption, similar to that seen following the use of the arsphenamine compounds, developed after injections of sodium aurothiosulphate. The procedure, a modification by Dr. J. Patterson of a test described by R. Coquin, is as follows: The incinerated material is treated with excess hydrochloric acid, evaporated to dryness and ignited. After the ignited mass is extracted with water, the residue is dissolved in chlorine or bromine water, evaporated to dryness and ignited in a porcelain crucible. The residue is extracted with aqua regia, evaporated to dryness and again ignited. The violet coloration is shown with as little as 0.001 mg. of gold. Control experiments, carried out with apparently normal skin from four patients with lupus erythematosus who had received a similar amount of sodium aurothiosulphate, gave completely negative results. Thus it is noted that gold was found only in the skin of patients showing a definite reaction. In one of the cases described the reaction was eczematous, while in the other two it was an acute toxic erythema, followed by pigmentation in one. The literature on toxic reactions to sodium aurothiosulphate is reviewed, and on the basis of observations in his three cases, Wigley discusses the pathogenesis.

FURTHER OBSERVATIONS ON THE ETIOLOGY OF PAPULAR URTICARIA (LICHEN URTICATUS). R. HALLAM, Brit. J. Dermat. **44**:117 (March) 1932.

Observations in eleven typical cases of papular urticaria showed that hospitalization of the child at night only has a remarkable influence on the course of the disease. Reference is made to the observation by Jadassohn that in cases of Hebra's prurigo the condition cleared up in an inexplicable manner when the patient was admitted to the hospital. The article is concluded with the following statements: 1. Papular urticaria is an allergic manifestation. 2. As the complaint may be controlled by detaining the child in the hospital for the night only, the exciting cause is probably associated with the sleeping garments at home. 3. A food factor is not the exciting cause.

AUTOHEMOTHERAPY. N. BURGESS, Brit. J. Dermat. **44**:124 (March) 1932.

Following a brief review of the literature, Burgess describes some experiments which were carried out in an attempt to throw light on the mode of action of autohemotherapy. The technic used throughout his work was the intramuscular injection of freshly drawn whole blood. The subject was investigated under the following headings: (1) effect of injections of whole blood on the total leukocyte count; (2) the hemoclasic crisis; (3) the effect of injections of whole blood on the sedimentation rate of the red cells, and (4) the effect of injections of whole blood on the urinary proteose. The results are presented in tables, and on the

basis of this investigation he makes the following conclusions: 1. The action of injections of whole blood does not depend on the production of leukocytosis. 2. The hemoclasic crisis is not a satisfactory test for allergy. In the cases examined no relation between injections of whole blood and the hemoclasic crisis was discovered. 3. Injections of whole blood had no effect on the sedimentation rate of the red corpuscles as estimated by the method of Zeckwer and Goodell. 4. Proteose was obtained from the urine of normal persons and of those suffering from various dermatoses. No constant effect on the production of proteose by a single injection of whole blood could be demonstrated.

WIEN, Chicago.

COLLAGENOUS DEGENERATION: A CASE FOR DIAGNOSIS. H. C. SEMON, Proc. Roy. Soc. Med. **25**:1317 (June) 1932.

A man, aged 36, presented only one type of eruption, the elements of which could be analyzed only at the spreading margins, and best, perhaps, on the buttocks and thighs. Elsewhere the lesions had become conglomerate, and were so faintly marked as to defy description. On the base of the neck and over the pomum adami, where the signs of the eruption were first noted, the condition had entirely involuted, leaving a remarkable inelastic texture, as seen temporarily after edema of the skin or in old age. Each lesion was oval, its long axis, which ranged from one-fourth to one-half inch, being disposed horizontally. A delicate mauve was the prevailing tint of the more recent lesions, but in places where they had become absorbed into the sheetlike agglomeration on the trunk, the color was brownish. Here, too, all the follicles were rendered extremely prominent by the apparent exudation, and almost pinned the epidermis down like "buttons on a mattress," and at a few feet produced the appearance of coarsely grained leather. The individual small elements were smooth, raised, but scarcely palpable, lesions. There was no scaling or other change suggestive of a disturbance of the malpighian body. The general effect was one of edema or exudate into the epidermis and of perifollicular distribution.

The epithelial layer was for the most part flattened, owing to the disappearance of the rete cones. The collagenous tissue arose immediately beneath the epidermis and was relatively acellular; its bundles were indistinct, suggesting the effect of ground glass, under a one-sixteenth inch objective, and stained poorly with van Gieson's stain. The elastic tissue, on the other hand, was well presented by Weigert's stain and presented no evidence of degeneration. The appearances suggested a form of collagenous degeneration of the skin.

EPIDERMOLYSIS BULLOSA WITH CUTIS HYPER-ELASTICA. A. BURROWS, Proc. Roy. Soc. Med. **25**:1317 (June) 1932.

A schoolgirl, aged 14, seen at the London Hospital, in association with the mother, stated that since birth she had had flexible skin, which became normal when released, and a particular susceptibility to injury over the bony prominences. The patient had always had cold, cyanosed hands, with a tendency to chilblains. When injured the skin tended to do one of two things: either develop large blisterlike lesions, often with the formation of bruises, or "split right down to the fat," making a deep and ugly wound. In one case, the patient had to be treated at the German Hospital for such a wound in the left knee, which became septic. There were the scars of injuries over both knees, above the left shin and over the left forearm. The skin itself had a silky, over-rolling feeling when palpated, and could be abnormally stretched. This feature was most marked at the elbows and knees, where, if the skin were stretched and released, it went rapidly back to normal, almost as though it were elastic. The elasticity was notable on both sides of the body. The patient had laxness of the joints, which was particularly noticeable in the thumbs of each hand, which could perform the usual "double-jointed" movements, and could be greatly hyperextended.

GUY, Pittsburgh.

CONGENITAL ICHTHYOSIFORM EPIDERMOLYSIS. S. LAPIERE, Ann. de dermat. et syph. **3**:401 (May) 1932.

Two cases of congenital icthyosiform erythroderma, one the typical dry form and the other a bullous variety, are reported and discussed in detail, with special emphasis on the histology. The whole subject of the congenital icthyotic group of dermatoses, in which there has been so much confusion in nomenclature, is critically reviewed in the light of the two cases reported.

GANDY, Houston, Texas.

SEVEN CASES OF GENERALIZED ARGYRIA. GERNEZ, HOUCKE and CUVELIER, Ann. de méd. lég. **4**:251, 1932.

A veritable epidemic of argyria was observed by the authors in patients suffering from pulmonary tuberculosis treated with collargol. The usual symptoms of nausea, vomiting, anorexia, abdominal pain and diarrhea accompanied the intoxication. These symptoms continued for several months after discontinuance of the injection of collargol. Silver was not found in the urine or in the blood, but it was present in the hair and in the nails of one patient. Chemical analysis of 10 cc. of bile did not reveal silver, but spectroscopic examination of this material yielded positive results. The coloration developed after a latent period of about one year, during which time there were no other symptoms except digestive disturbances and progressive asthenia.

H. S. THATCHER. [ARCH. PATH.]

TREATMENT OF CUTANEOUS TUBERCULOSES BY LOCAL INJECTIONS OF A GOLD COMPOUND: RESULTS AND ANAPHYLACTIC ACCIDENTS. GOUGEROT and BURNIER, Bull. Soc. franç. de dermat. et syph. **39**:691 (June) 1932.

Several patients afflicted with various tuberculous conditions of the skin were treated by means of local injections of a gold compound, after the method of Monash and Traub, with the following results: seven patients with lupus erythematosus, six cured, one improved; three patients with erythema induratum, cured; one patient with granuloma annulare, cured; one patient with lupus miliaris disseminatus, improved; one patient with ulcerative tuberculosis, cured, and one patient with tuberculous gumma, condition checked.

The authors' conclusions may be listed as follows: 1. This method deserves a place alongside general therapy with gold compounds. 2. It has special value in cases that have failed to respond to the intravenous administration of gold compounds. 3. It is particularly indicated in tuberculous diseases limited to the skin. 4. Apart from rare local or general reactions, it is well supported. 5. Care must be exercised with this method, since anaphylactic reactions do occur, as manifested in the patient with lupus miliaris disseminatus by chills, fever and vomiting, and in one with erythema induratum, by a generalized erythroderma.

ACHROMIC (OR INVERSÉ) PITYRIASIS VERSICOLOR. M. E. COHEN-HADRIA, Bull. Soc. franç. de dermat. et syph. **39**:774 (June) 1932.

A young girl who had had considerable exposure to the sun in a bathing suit exhibited a typical pityriasis versicolor on the flanks and lumbar region, but "achromic" lesions on the exposed parts — the neck and the upper part of the back. Instead of the classic brownish plaques on a white background, the lesions appeared as whitish spots on a hyperpigmented background. The author has seen several such cases, and proposes for them the term pityriasis versicolor inversé.

PURPURA WITH BULLAE DUE TO GOLD. M. E. GRIVEAUD, Bull. Soc. franç. de dermat. et syph. **39**:822 (June) 1932.

In a man, aged 25, who was being treated for lupus erythematosus, a second injection of gold was followed in twenty-four hours by the appearance of purpura on the extremities, accompanied by bullae on the hands and feet, an unreported phenomenon. The whole eruption cleared up in three weeks.

GANDY, Houston, Texas.

INDURATION OF THE SKIN IN THE NEW-BORN. H. SLOBOSIANO, Nourrisson **20**:197 (July) 1932.

Induration of the skin of the face often follows trauma due to the pressure of forceps blades. Such induration may cause pain when the infant tries to nurse and a refusal of food. Indurations of the skin over the trunk or extremities are more likely to be caused by a chilling of the cutaneous surface at or shortly after birth. The fatty acids (oleic, palmitic and stearic) of the subcutaneous tissue in the new-born are present in different proportions than in the adult; palmitic acid accounts for 29 per cent of the fat of the new-born as compared with 8 per cent in the adult. The water content of the subcutaneous tissue is much higher in the new-born than in the older infant or adult. These factors render the skin of the new-born much more susceptible to the effects of exposure to cold, and indurations are more likely to develop.

McCLELLAND, Cleveland. [AM. J. DIS. CHILD.]

SYPHILIS OF THE LUNG. B. DE CARVALHO, J. de syph. e urol. **3**:188 (Aug.) 1932.

The author reports the case of a Brazilian man, aged 35, who while apparently in good health suffered from a serious hemoptysis. Roentgen examination of the chest showed lesions in both lungs. The Wassermann test was strongly positive. Injections of bismuth produced a gradual disappearance of the lesions. The patient gained 14.5 Kg. (31.9 pounds) in weight in eight months.

GRANULOMA VENEREA. C. STAJANO and A. STABILE, Rev. méd. latino-am. **18**:18 (Oct.) 1932.

Granuloma venerea was unknown in Uruguay until 1915. It was usually diagnosed as vulvar esthiomene, tuberculosis or syphilis. The author distinguishes the following clinical varieties: (1) chancriform; (2) serpiginous and proliferating; (3) papulohypertrophic, simple or ulcerative; (4) pseudo-elephantiasic, and (5) associated forms. A 1 per cent solution of sodium and antimony tartrate is specific, but in some cases electrocoagulation of the lesions and roentgen therapy are useful.

PARDO-CASTELLO, Havana, Cuba.

THE DEMONSTRATION OF ELEMENTS IN THE TISSUES: III. ARGYROSIS, ESPECIALLY CONCERNING THE DEMONSTRATION OF SILVER IN THE SKIN BY MEANS OF THE SPECTROSCOPE. WALTHER GERLACH and WERNER GERLACH, Dermat. Wchnschr. **95**:1497 (Oct. 15) 1932.

A method for determining metals in tissue by means of the spectroscope is discussed and described. In three instances of argyria, the authors were able to demonstrate the typical spectroscopic lines of silver. The tissue is volatilized by means of a high frequency spark.

SKIN TESTS BY MEANS OF PIGMENT WHEALS. ROMAN VON LESZCZYŃSKI, Dermat. Wchnschr. **95**:1508 (Oct. 15) 1932.

The author made intracutaneous injections of a 2: 10,000 aqueous solution of trypan blue in about one hundred normal persons, using various portions of the body to determine the difference in the behavior of different areas. He concludes that the production of a wheal by means of trypan blue may be developed into a functional test of the reticulo-endothelial system of the skin.

FEER'S DISEASE. M. FELLNER, Dermat. Wchnschr. **95**:1541 (Oct. 22) 1932.

A typical case of Feer's disease (juvenile acrodynia) is described in a 1½ year old boy. The only unusual feature was the presence of an enlarged liver. The condition cleared up under treatment with injections of liver extract, and the author believes that dysfunction of the liver may play a part in other cases, in spite of the absence of hepatic symptoms.

MICROSCOPIC EXAMINATION OF CULTURES OF FUNGI. W. ENGELHARDT, Dermat. Wchnschr. **95**:1546 (Oct. 22) 1932.

Small amounts of the material to be cultured are planted on Petri dishes in which the culture medium is thinly spread. When the cultures are just starting to grow, a small area of the medium is cut out and placed on a slide and covered with a cover glass. This allows a satisfactory microscopic examination of the culture.

THERAPEUTIC MALARIA. E. MARTIN, Dermat. Wchnschr. **95**:1548 (Oct. 22) 1932.

The author points out the possible dangers of malarial therapy. He emphasizes the fact that the cure of this disease is not always as certain as might be desired and advises the use of every modern test to verify the cure. Furthermore, the possibility of aggravating any preexisting condition must be guarded against.

HISTOLOGIC STUDY OF A BLOOD TUMOR-LIKE LESION OF NEVOID ORIGIN PRESENTING THE STRUCTURE OF A HEMANGIO-ENDOTHELIOMA. M. J. PER, Dermat. Wchnschr. **95**:1569 (Oct. 29) 1932.

A man, aged 29, presented a walnut-sized, verrucous, red growth on the external part of the ear. It had been present for twenty-one years, and it had grown a little from time to time. It was excised, and microscopic study showed many new blood vessels as well as nests and strands of endothelial cells. The author concludes that it was a nevus hemangio-endotheliomatosus.

CONGESTION DERMATOSIS FOLLOWING INJECTIONS INTO VEINS. OTTO MEYER, Dermat. Wchnschr. **95**:1574 (Oct. 29) 1932.

Pruritic dermatitis may accompany chronic phlebitis of the leg. Injection into parts of the compensatory circulation under the impression that they are varicose veins leads to an intensification of the symptoms.

THE SPECIFICITY OF THE LYMPHOGRANULOMA INGUINALE REACTION. W. FREI, Dermat. Wchnschr. **95**:1575 (Oct. 29) 1932.

Frei believes that a positive intracutaneous reaction occurring forty-eight hours after inoculation is always specific for lymphogranuloma inguinale. He reviews the three nonspecific reactions which have been reported in the literature and considers them to have been errors in interpretation. A false negative reaction does occur occasionally, and the author briefly points out the circumstances which may cause it.

STUDIES OF PSORIASIS. WILHELM RICHTER, Dermat. Wchnschr. **95**:1597 (Nov. 5) 1932.

The author studied sixty-five psoriatic patients from the standpoint of the secretion of internal glands. To determine dysfunction he used the interferometric destructive reaction (*interferrometrische Abbaureaktion*) of Abderhalden. He concludes that the suprarenal hormone is frequently at fault.

PRIMARY TUBERCULOSIS OF THE SKIN OF AN ADULT. PER L. ROTNES, Dermat. Wchnschr. **95**:1605 (Nov. 5) 1932.

In a woman, aged 30, who had previously been in good health, an ulcerated lesion of the upper lip developed, with an associated lymphadenopathy and an eruption resembling erythema nodosum. The Wassermann reaction was negative, and no spirochetes were found in a dark-field examination of material from the ulcer. The Pirquet test was strongly positive (vesicular reaction). Tubercle bacilli were recovered from material aspirated from the cervical glands. There was no evidence of tuberculosis of the lungs. The patient's fiancé was found to have open tuberculosis of both lungs.

TREATMENT OF DISEASES OF THE NAILS. J. SCHÜTZ, Dermat. Wchnschr. **95**:1608 (Nov. 5) 1932.

A patient with a marked subungual hyperkeratosis was markedly improved by daily massage of the nails in warm hydrogen dioxide.

ARE THERE FORMS OR STAGES OF THE CAUSATIVE AGENT OF SYPHILIS OTHER THAN THE SPIROCHETE? F. JAHNEL, R. PRIGGE and M. ROTHERMUNDT, Dermat. Ztschr. **64**:7 (June) 1932.

From a review of the literature and from their own research, the authors conclude:

1. The syphilitic virus may be demonstrated in the organs of syphilitic animals by the inoculation of tissue into fresh animals, though microscopic examination of the organs fails to reveal spirochetes.

2. This observation is true during the primary and latent stages of manifest syphilis in rabbits, as well as in the asymptomatic syphilis of rabbits, guinea-pigs, white mice and white rats.

3. This does not necessarily mean that the syphilitic virus is present in an invisible form, but rather that the number of spirochetes present is so small as to make their demonstration extremely difficult. A variation of type of the spirochete certainly does not occur.

4. Filtration experiments rule out the possibility of a filtrable form of the syphilitic virus.

A SPECIFIC CHANGE IN THE VEINS IN EXPERIMENTAL FRAMBESIA OF RABBITS (SUMATRA STRAIN). ERICH HOFFMANN, Dermat. Ztschr. **64**:29 (June) 1932.

Hoffmann is convinced that frambesia and syphilis are similar but not identical. Frambesia is characterized in experimental animals by a tendency toward granulomatous lesions, such as the papillary primary and granular periorchitis. The author describes a nodular phlebitis which occurs as part of the periorchitis in rabbits. He believes that this phlebitis is specific for frambesia.

SUPERFICIAL TERTIARY SYPHILITIC INFILTRATION OF THE SKIN. RUTH LINDEMANN, Dermat. Ztschr. **64**:51 (June) 1932.

A patient is described whose tertiary syphilid was a superficial infiltration of the palms and the sides of the trunk. The condition resembled eczema and had been so treated for a considerable period. Serologic examination gave positive results, and prompt cure followed antisyphilitic therapy.

TAUSSIG, San Francisco.

IRRITANT ACTION ON THE PROTECTED EYES OF ROENTGEN AND ULTRAVIOLET RAYS DIRECTED TO DISTANT PARTS OF THE BODY. K. KIKAI, Klin. Monatsbl. f. Augenh. **88**:478 (April) 1932.

Exposure to roentgen and ultraviolet rays is known to cause general symptoms besides the local appearances. To find the cause of this with reference to the eye, Kikai exposed the backs of rabbits to varying doses of roentgen rays and to the Alpine sun lamp for varying lengths of time. Histologic examination of the eyes, which were well protected during the experiments, showed the same ocular changes as those obtained by von Szily after intravenous, intraperitoneal and subcutaneous injections of catabolic bodies.

These local ocular changes developed usually two or three weeks after the exposures, indicating that a certain length of time is required before the active substances can form by destruction of endogenous tissues. Focal infiltrations in the choroid and edema of the ciliary processes were found. Variations of the intraocular tension, observed by Krasso, Salinger and Thiel after exposure to roentgen

rays and attributed to irritation of the sympathetic nerve, may be due to the action of parasympathetic catabolic bodies. Kikai arrived at this opinion because of the protracted effect of one exposure, because the second eye, although not exposed, showed a parallel reaction with the first and because repeated exposures produced a more distinct and more prolonged decrease of the tension.

K. L. Stoll. [Arch. Ophth.]

Treatment of Erythrodermia Desquamativa. Herbert Schönfeld, Monatschr. f. Kinderh. **54**:268, 1932.

The author has reduced the mortality rate from 30 per cent to 7 per cent in a series of 120 cases. The procedure consists in maintaining the child's nutrition by a diet in which a minimum of two thirds consists of breast milk. The remaining third is a buttermilk-rice gruel mixture. Excellent results were obtained by the injection of from 10 to 20 cc. of blood, which may be repeated every two or three days. This injection may be given intramuscularly, and in the more severe cases, intravenously.

Gerstley, Chicago. [Am. J. Dis. Child.]

Severe Trophic Corneal Damage in a Case of Arsphenamine Dermatitis. H. Sauferlin, München. med. Wchnschr. **79**:1476 (Sept. 9) 1932.

A case report of this unusual complication is preceded by a survey of the literature on like conditions, and a comprehensive bibliography is appended. The outstanding feature of the author's case was the severe damage to the cornea without previous visible inflammation of the eye, and the surprising rapid involvement in spite of careful ophthalmologic supervision. Because of the absence of reaction, together with the finding of an ulcer involving the entire thickness of the cornea, a diagnosis of trophic corneal abscess was made by the ocular department. The patient, aged 43, received one injection of 0.3 Gm. and seven of 0.45 Gm. of neoarsphenamine, together with fifteen injections of bismuth in a period of six months. The day following the last injection of arsphenamine a rash appeared on both arms which spread in two days to the neck, breast and face. Local treatment did not help. The tongue was swollen, and the mucous membrane of the mouth was reddened. The temperature was 39 C. (102.2 F.) and the pulse rate, 100, which increased to 39.5 C. (103.1 F.) and 110, respectively, on subsequent days. There was a mild conjunctivitis not involving the cornea, which responded to treatment quickly with some recurrence. Six weeks later the patient suddenly complained of a severe pain in the right eye. Examination revealed a perforation of the cornea parallel to the limbus from 11 to 12 o'clock with a prolapsed iris. A fine powder-like clouding of the entire cornea was noted. The iris prolapse was excised, and a conjunctival flap thrown over the perforated area. The dermatitis subsided under treatment with injections of sodium thiosulphate. A visual acuity of 5/60 was obtained in the affected eye. The author believes that the reaction was due to accumulative effects of the arsphenamine. The conjunctivitis is construed as the first sign of an overdose.

L. L. Mayer. [Arch. Ophth.]

Bacteriology of Lymphogranulomatosis and Mycosis Fungoides. Natalia Busny, Virchows Arch. f. path. Anat. **280**:626, 1931.

In one hundred and forty cases of lymphogranulomatosis and five of mycosis fungoides, the author cultivated from the blood and involved tissues a bacterial organism that is morphologically and culturally identical in the two diseases. The ordinary bacteriologic mediums and methods were used. Within from twelve to twenty-four hours the organism appears in cultures as a slender, acid-fast bacillus. In from twelve to twenty-four hours more it is transformed into gram-positive cocci that are arranged in pairs, tetrads and short chains. In an additional twelve to twenty-four hours the cocci have increased in size and have arranged them-

selves in staphylococcus-like clusters. Injection of the acid-fast bacillary forms into guinea-pigs leads to the formation of lesions like those in the human diseases. From such lesions the pleomorphic organism can again be cultivated. For the successful inoculation of guinea-pigs a larger amount of inoculum is necessary than in the case of the tubercle bacillus. If the coccoid forms are injected into guinea-pigs, only the acid-fast bacillary form is obtained from the animal after forty-eight hours. The localization of the organism in the experimental lesions is identical in both lymphogranulomatosis and mycosis fungoides. The author considers the organisms specific for lymphogranulomatosis and mycosis fungoides. Further immunobiologic investigation is necessary to determine whether the organisms from the two diseases are identical and to determine their relationship to the tubercle bacillus.

LOCALIZED AMYLOIDOSIS WITH MACROGLOSSIA. G. GERSTEL, Virchows Arch. f. path. Anat. **283**:466, 1932.

In a woman, aged 52, who had always been well, there developed "over night" marked swelling and hardening of the gums and tongue. The swelling quickly reached its maximum intensity and persisted until death two years later. Thickening and hardening of the skin of the neck developed more gradually and continued progressively until death. The gross anatomic diagnosis was diffuse amyloidosis of the tongue, buccal tissues, upper part of the esophagus and intestine, and of the skin, subcutaneous tissues and muscles of the neck. Organs commonly involved in generalized amyloidosis, namely, the spleen, liver, kidneys, suprarenal glands and lymph nodes, contained no amyloid. The suprarenal glands and the lymph nodes of the mesentery and elsewhere were surrounded by amyloid, but the organs themselves were free from it. The gluteal muscles, the diaphragm and the heart muscle contained much amyloid. The amyloid material formed thick sheets or large nodular masses at the junction of submucosa and muscle, of connective tissue and muscle, or of nerves and surrounding tissue. Thorough microscopic examination of the various tissues and organs of the body revealed no suppurative or inflammatory process to which the amyloidosis might be ascribed. Lubarsch, who has reported three cases, noted as characteristic the occurrence in situations not usually involved in generalized amyloidosis, the absence of amyloid infiltration in organs usually involved in the generalized form, and the absence of any suppurative process or other underlying disease to which the condition might be ascribed. He also noted that the chemical reactions of localized amyloid are usually atypical. Common manifestations are: involvement of the skin over the infiltrated deeper tissues (amyloid pseudoscleroderma), involvement of the voluntary musculature (amyloid pseudomyotonia) and tumor-like enlargement of the infiltrated organ or tissue (amyloid pseudotumor). Pick, from whose institute the present report comes, believes that these manifestations together with the congo red test should make clinical diagnosis of the condition possible.

O. T. SCHULTZ. [ARCH. PATH.]

RESISTANT SYPHILIS AND SULPHUR COMPOUNDS. K. HÜBSCHMANN, Česká dermat. **13**:79, 1932.

In his persistently seropositive cases, the author tried to combine specific treatment with certain sulphur preparations. Best results were obtained from intravenous injections of sodium thiosulphate in doses larger than those advocated by Beinhauer and Jacob (from 1 to 2 Gm. of thiosulphate three times a week, or a total of from 10 to 20 Gm. per course). Of ten patients, seven showed a marked improvement with the combined treatment, which was usually noticeable after from four to eight injections. However, some of the patients had a relapse or positive reaction when the specific treatment was discontinued and they were getting thiosulphate alone. The blood serum of patients treated with thiosulphate showed an increased stability of colloids and a greater resistance of colloids to alcohol.

DERMOLUETIN REACTION IN CONGENITAL SYPHILIS. OLGA VALENTOVA, Česká dermat. **13**:91, 1932.

The author tabulates the results of 102 dermoluetin tests applied to children at the dispensary in Prague. First group: Children with clinical manifestations of syphilis and a positive serum reaction.

(*a*) No previous treatment, 4.

(*b*) Under treatment, 13.

Results of luetin reaction:

(*a*) 3 strongly positive (2 keratitis, gumma). 1 weakly positive (neurosyphilis).

(*b*) 10 positive (keratitis). 3 negative (keratitis; chorioretinitis; idiocy).

Second group: Children with positive serum and without clinical symptoms. All under treatment.

(*a*) 12 never had symptoms.

(*b*) 8 symptoms disappeared under treatment.

Results of luetin reaction:

(*a*) 6 weakly positive and 6 negative.

(*b*) 2 positive (cured keratitis), 4 weakly positive and 2 negative.

Third group: Children free from symptoms and with negative serum.

(*a*) Syphilis in parents and other children 50.

(*b*) 8 children whose conditions cleared up under treatment clinically and serologically.

Results of luetin reaction:

(*a*) 1 strongly positive (mother 4 plus). 2 weakly positive. 47 negative.

(*b*) 2 positive (healed gumma). 6 negative.

Fourth group: Normal children for control. All gave negative reactions.

The author considers the positive results in the third group as the most important and as speaking in favor of the test that may help to clear the question as to whether or not to treat patients with latent congenital syphilis.

PATHOGENESIS OF ALOPECIA AREATA. VLASTA ŘIHOVÁ, Česká dermat. **13**:96 and 107, 1932.

The author discusses the parasitic, trophoneurotic, reflex and endocrine theories, but favors the view that alopecia areata is the symptom of a systemic disease, namely, a disturbance of internal secretions. The first part of the paper deals with alopecia areata caused by hypothyroidism and hyperthyroidism, by ovarian disturbances of puberty and menopause and by an enlarged hypophysis, and the author discusses syphilitic alopecia, which is considered by many to be identical pathogenically with alopecia areata.

The second part of the paper is devoted to a clinical, experimental and histologic study of thallium alopecia and its relation to alopecia areata. Clinically, the picture of thallium alopecia is identical with that of alopecia areata caused by hypothyroidism. In the described case of thallium poisoning (rat poison taken with suicidal intent), the patient happened to take exactly the epilating dose. Besides a total loss of hair, she showed a positive Hertogh sign, decreased basal metabolism and leukonychia striata involving all the finger-nails. Ovarian disturbance was evidenced by intermenstrual flow. Results of general examination pointed overwhelmingly to a disturbance of the thyroid gland.

By experiments on rats, the author brought out the fact that the diet has a great influence on the action of thallium. A diet rich in casein and vitamin A delays and decreases the epilating effect of thallium. The diet may be one of the exogenous factors influencing thyroid hormone, increasing or decreasing its peripheral effect.

Histologic study brought out the following facts: Thallium has a definite influence on the vitality of epidermal cells. The cells of the hair bulbs are the most sensitive; those of the nail matrix and skin are less so. Thallium hastens the normal shedding of hair. Only in small repeated doses does it lead to atrophy

and disappearance of the hair follicles. The author found no degenerative changes in the first stage of hair regression as described by Truffi. Forty-one photomicrographs illustrate this part of the paper. The author concludes that thallium causes alopecia indirectly through its action on the endocrine system. Thallium alopecia is, therefore, not only clinically but also pathogenically closely related to alopecia areata and is regarded by the author as a systemic disease.

INSULIN TREATMENT OF ULCUS CRURIS. J. DOHNÁLOVÁ, Česká dermat. **13**:103, 1932.

The author reports good results obtained from the application of a 10 per cent insulin ointment in two cases of ulcus cruris gangraenosum in diabetic patients, in four cases of second and third degree burns and in one case of gangrenous ulcer in a patient with pemphigus. In seven nondiabetic patients with ulcus cruris the condition, which had resisted all previous therapy, responded to insulin. There was only one failure.

ECZEMA OF HANDS FROM GOOSE FEATHERS. MARIE RUNTOVÁ, Česká dermat. **13**:129, 1932.

The patient had two attacks of eczema. The first one was brought on by Lux soapsuds, and the second by goose feathers.

SPINKA, Texarkana, Texas.

RESISTANCE OF PERIPHERAL CAPILLARIES OF THE HUMAN BODY: PHYSIOLOGIC DATA. H. KOGAN and P. SNYAKIN, Sovet. clin. **17**:46, 1932.

Following previous investigations by the authors by means of the vasotonometer, which revealed that the capillary pressure is different in various pathologic conditions and depends on a great number of factors, the authors have examined the capillary resistance in parts all over the body in normal persons. A drawing of a human body with figures indicating the pressure in millimeters of mercury gives the average physiologic resistance of the peripheral capillaries.

HEMORRHAGIC DIATHESIS AND THE PHENOMENON OF THE "BIBLICAL" BLOOD SWEATS. G. K. LAVSKI, Sovet. clin. **17**:48, 1932.

The author describes a case of a woman, aged 24, a student, who since school age had suffered from occasional blood sweat on the nose and the left hand, the frequency and intensity of which was somewhat dependent on increased excitability, particularly in connection with expected examinations. In 1924, after a psychic upset produced by the suicide of a close friend, there was a blood sweat of the left hand lasting two hours. The skin was examined and found to be intact. Blood sweats took place also on the left foot.

The patient was constitutionally psychopathic with schizophrenic, hysterical and psychasthenic reactions. She believed that she could predict the future and converse with the spirits of great men. Her father was alcoholic and her mother was neurasthenic and had pulmonary tuberculosis. Three children in the family were also of a psychopathic constitution. The patient's younger sister had purpura haemorrhagica. The prolonged bleeding time of eight and one-half minutes, and the diminished number of blood platelets associated with occasional severe nosebleeds indicated a hemorrhagic diathesis.

THE INFLUENCE OF PERIARTERIAL SYMPATHECTOMY ON LEUKOCYTES: SURGICAL PROCEDURES ON THE SYMPATHETIC NERVOUS SYSTEM. I. N. ISHTSHENKO and O. V. PROSKUR, Sovet clin. **17**:211, 1932.

The authors have examined the blood from both lower extremities in four patients who underwent femoral sympathectomy, and found in three of them distinct leukocytosis, more marked in the extremity operated on than in the healthy

one. Leukocytosis was due to an absolute increase in neutrophils, with distinct lymphopenia in the blood of the extremity operated on and without lymphopenia in the blood of the healthy extremity. The leukocytosis appeared several hours after a period of leukopenia which followed the operation.

This observation enables one to predict to some extent the effect of an operation. The authors have utilized this knowledge in the treatment of beginning spontaneous gangrene of the lower extremities. If arterial sympathectomy was followed by leukocytosis, there was hope that an operation on the spinal nervous system (sympatectomia lumbalis) would be of value. If the arterial sympathectomy was not followed by leukocytosis, the more radical operation was contraindicated.

Leukocytosis is one of the factors that explain the therapeutic effect of sympathectomy. It explains also the finding of Leriche that ulcers of the extremities become sterile within forty-eight hours after the operation.

BLOOM, New York.

THE RADIOLOGIC TREATMENT OF MALIGNANT GROWTHS IN THE BUCCAL CAVITY. ELIS BERVEN, Acta radiol. **13**:213, 1932.

In carcinoma of the oral cavity a combination of radium and endothermy for the treatment of the primary tumor is used at Radiumhemmet, Stockholm, with a combination of radium and conservative surgical procedures for the lymph node-bearing areas. In their experience radium has proved superior to the quality of roentgen irradiation now available. The author regards the greatest gain of recent years as existing in the introduction of the teleradium technic of treatment at a distance and the more widespread use of needle implants in combination with endothermy. Treatment at Radiumhemmet consists of routine initial teleradium treatment of the primary tumor and, after the lesion has become cleaner, smaller and better defined, coagulation by endothermy, with simultaneous implantation of needles into the tissue surrounding the coagulated area. The lymph node areas are treated by the teleradium technic at the time of treatment of the primary tumor which is followed by surgical dissection of any movable, easily operable glandular metastases remaining after teleradium treatment. Of 278 patients suffering from carcinoma of the buccal cavity, 27 per cent are free from symptoms from five to eleven years after treatment. Details of statistics for the various types and locations of lesions treated are also given.

RADIUM THERAPY IN CANCER OF THE LIP FROM THE POINT OF VIEW OF METASTASES. E. COLLIN, Acta radiol. **13**:232, 1932.

The author presents statistics of one hundred and one cases of cancer of the lip, in all of which the patients were treated by radium, and were subsequently observed for at least three years. According to the treatment given, the cases may be divided into three groups: those in which there was no prophylactic roentgen treatment of the regional glands; those in which such treatment was given, with light filtration, and those in which the same roentgen treatment was given, with heavy filtration. With all due reservation for the relatively small number of cases on which his conclusions are based, the author finds that the best results are obtained when the radium treatment of the lesion itself is supplemented by prophylactic roentgen treatment, with soft rays, of the regional glands; that the result from radium treatment alone is almost as good, and that with hard ray roentgen treatment of the glands the result is decidedly inferior. His statistics show a total rate of cure of about 80 per cent.

WIEDER, Milwaukee.

Society Transactions

CLEVELAND DERMATOLOGICAL SOCIETY

J. R. DRIVER, M.D., *Reporter*

Regular Meeting, Sept. 22, 1932

E. W. NETHERTON, M.D., *Presiding*

PARAPSORIASIS GUTTATE. Presented by DR. H. F. DE WOLF.

D. J., a white girl, 4 years of age, from the service of Dr. H. N. Cole and Dr. J. R. Driver at Cleveland City Hospital, presented an extensive maculopapular eruption consisting of lesions varying in diameter from 2 mm. to 1 cm. They were markedly scaly and a coppery brown. There were no subjective symptoms. The eruption was of one year's duration and had resisted treatment.

DISCUSSION

DR. H. F. DE WOLF: We presented the case because some textbooks state that parapsoriasis does not occur in persons under 12 years of age.

BULLOUS PURPURA. Presented by DR. H. G. MISKJIAN.

M. A., a white woman, an Italian, aged 52, from the service of Dr. H. N. Cole and Dr. J. R. Driver at Lakeside Hospital, presented an eruption on the legs of two months' duration. She had not taken any drugs, including iodides, except, occasionally, a cathartic containing phenolphthalein. There was no history of previous attacks.

Examination showed that the eruption was limited to the legs, on the upper portion of which the lesions were bright red and petechial. Lower, there were a few larger patches of purpura, from 1 to 1.5 cm. in diameter, with an irregular contour. Some of them were surmounted by a bulla filled with a serosanguineous fluid. The bullous lesions were present both on the anterior and the posterior surfaces of the lower half of the legs, but they were more numerous on the anterior surface. Besides, both legs showed the remains of healed elements. These had a diffuse, brownish pigmentation on the periphery; their centers were depressed and distinctly atrophic. Slight pigmentation was present also in the center of many of these healed lesions. There were varicose veins on both legs. In a few areas the subsequent development of the bullous lesions resulted in purulent crusts which, when removed, revealed necrotic superficial ulcers. Urinalysis showed a large amount of sugar. The Wassermann test of the blood was negative.

DISCUSSION

DR. H. J. PARKHURST: Regardless of the fact that there is a negative history concerning the ingestion of iodides, the eruption resembles an iodermia, and it is possible that in a susceptible person the eruption could be produced by the use of iodized salt.

DR. J. R. DRIVER: Many dermatoses become hemorrhagic on the lower extremities and do not show this phenomena on the trunk or upper extremities. It is not unusual to find lichen planus with bullous lesions on the legs and none on other parts of the body. My interpretation of the condition would be that it is

probably rheumatic purpura with secondary ecthymatous lesions due to contamination of the ruptured bullae.

DR. H. G. MISKJIAN: I considered the possibility of an atrophic purpura such as has been described by Pospelow. However, for the present one would have to diagnose the condition as necrotic purpura, the etiology of which cannot be determined by studies made.

ESTHIOMENE (LYMPHOGRANULOMA INGUINALE). Presented by H. F. DE WOLF.

J. M., a colored woman, aged 46, from the service of Dr. H. N. Cole and Dr. J. R. Driver at Cleveland City Hospital, had had a hysterectomy on account of fibroids performed at Cleveland City Hospital in 1926, at which time the Wassermann test of the blood was strongly positive. During the spring of 1927 she noticed that the vulva had become greatly swollen and painful. There were several attacks and remissions of this condition, each attack becoming progressively more severe, resulting in marked swelling and elephantiasis of the labia majora; with the formation of numerous sinuses on the vulva, perineum and buttocks. Some of these sinuses had healed, leaving scars. When last seen, the patient had numerous discharging sinuses, marked enlargement of the labia, with hard, board-like infiltration of the surrounding tissues. There was apparently no involvement of the inguinal lymph nodes.

The Wassermann test of the blood and precipitation tests for syphilis were strongly positive. Examination of the spinal fluid revealed 33 cells, a positive reaction for globulin and a strongly positive Wassermann reaction. Smears for gonococci and Bacillus tuberculosis were negative. Cultures had been negative for fungi. The tuberculin test was positive with a dilution of 1:100,000. The Frei test was weakly positive. A roentgenogram of the chest was negative for tuberculosis. Roentgenograms of the lumbosacral vertebrae and pelvis were negative for destructive changes in the bones. The amount of hemoglobin and the differential cell count were within normal limits. Antisyphilitic treatment consisting of arsphenamine and protoiodide given for a month produced no change in the lesions.

DISCUSSION

DR. H. F. DE WOLF: The clinical picture presented by this case fits in well with the diagnosis of esthiomene, which, as I understand it, may be due to various causes. While as yet one cannot say with absolute certainty that this is a case of lymphogranuloma inguinale, the clinical picture closely resembles that in cases of this condition which have been described in the literature. Personally, I do not think that this process is due to syphilis or tuberculosis. We shall treat the patient with antimony and potassium tartrate and continue to make Frei tests at intervals in order to see whether a provocative reaction to the Frei test will develop.

MULTIPLE SARCOID-LIKE LESIONS OF THE SKIN. Presented by DR. H. F. DE WOLF.

S. W., a colored man, aged 29, from the service of Dr. H. N. Cole and Dr. J. R. Driver at Cleveland City Hospital, had been presented before the Cleveland Dermatological Society on two previous occasions, on Oct. 17, 1929 (A Case for Diagnosis, ARCH. DERMAT. & SYPH. **21**:500 [March] 1930) and on Feb. 25, 1932 (Multiple Benign Sarcoid, ARCH. DERMAT. & SYPH. **26**:586 [Sept.] 1932). The eruption had persisted since March, 1929. It was present on the trunk, face, scalp and extremities. There were no lesions on the mucous membranes. The lesions consisted of small, indurated papules which became progressively larger until some areas showed indurated nodules up to 2 cm. in diameter. Many of the lesions followed the lines of cleavage of the skin, particularly in the region of the neck and chest, and from a distance resembled pityriasis rosea. However, the characteristic factors about the lesions were the marked induration and infiltration. Since the last presentation before the society, the patient had been seen by Dr.

Fred Weidman of Philadelphia, who believed that the condition was the exact counterpart of that seen in a colored patient (Klauder, J. V.: Multiple Sarcoid-Like Granulomas of the Skin of Undetermined Nature, ARCH. DERMAT. & SYPH. **12**:171 [Aug.] 1925). Necropsy in this case (Klauder and Weidman: ARCH. DERMAT. & SYPH. **13**:675 [May] 1926) proved the tuberculous origin of the lesions of the skin.

The patient has been on the salt-free Gerson diet for about six months, and a marked improvement has taken place, as evidenced by regression of many of the lesions and an increase in weight. On Dr. Weidman's suggestion that the process was due to avian tuberculosis, an enlarged inguinal lymph node was excised and inoculated into chickens, with negative results.

ARTERIAL EMBOLISM FOLLOWING INJECTION OF MERCURY. Presented by DR. H. F. DE WOLF.

L. K., a white boy, aged 16, from the service of Dr. H. N. Cole and Dr. J. R. Driver at Cleveland City Hospital, had been under treatment in the outpatient department since March, 1932. On Aug. 18, 1932, he received an intramuscular injection of 1 cc. of a 10 per cent suspension of mercuric salicylate in oil. The injection was given in the upper outer quadrant of the right buttock. Immediately following the injection, the patient complained of severe burning pain in the buttock at the site of the injection. The symptoms became increasingly more severe, and about three hours later it was necessary to hospitalize him. At the time there was a dull red swelling, approximately 10 cm. in diameter, and increased heat associated with motor paralysis of the sciatic nerve and extensive cutaneous anesthesia. Within a few days, the area became gangrenous, and a deep slough, 9 by 10 cm. in diameter and approximately 2.5 cm. deep, developed.

DISCUSSION

DR. H. T. PHILLIPS: How can accidents of this type occur if the usual precautions are taken to prevent injection into the blood vessels?

DR. J. R. DRIVER: If the point of the needle happens to be in the adventitia of the blood vessel, no blood can be aspirated, but the pressure of the injected material may break into the lumen of the vessel, producing an embolus.

DR. E. W. NETHERTON: What is the usual time required for recovery in cases of this type?

DR. J. E. RAUSCHKOLB: One patient was hospitalized for ten days two years ago. He was examined today, and there is no external evidence of the accident, but he still complains of weakness in the lower extremity on the affected side.

DR. J. R. DRIVER: I think that we are all familiar with the report Dr. John A. Gammel made on this condition several years ago (Arterial Embolism, *J. A. M. A.* **88**:998 [March 26] 1927). One of the patients in the cases reported in the paper had been reexamined recently and, after several years, still presented partial paralysis with toe-drop, making it necessary for her to wear a brace. A certain number of accidents of this type are unavoidable and are usually associated with serious end-results.

DR. SIDNEY LITTMAN: I have had a similar, less severe case following the injection of bismocymol.

LYMPHOGRANULOMA INGUINALE. Presented by DR. H. F. DE WOLF.

E. W., a colored man, aged 42, from the service of Dr. H. N. Cole and Dr. J. R. Driver at Cleveland City Hospital, presented a bilateral inguinal adenitis consisting of large matted glands producing a mass in each groin about the size of a hen's egg. Following numerous exposures, a urethral discharge had developed in June, 1932. There was no history of a penile lesion. A diagnosis of lymphogranuloma inguinale was made, and marked improvement resulted following the intravenous injection of a total of 73 cc. of a 1 per cent solution of antimony and

potassium tartrate. A Wassermann test of the blood was negative. Smears from the urethra were negative for gonococci. The Frei test was strongly positive with three different antigens. The Ito-Reenstierna test was negative. Cultures of aspirated pus from the inguinal glands were sterile on dextrose agar. Examination of smears of the pus for organisms gave negative results.

DISCUSSION

DR. J. E. RAUSCHKOLB: The primary lesion probably was intra-urethral, and perhaps many of the so-called cases of gonorrheal bubos reported in the older textbooks may have been instances of lymphogranuloma inguinale.

SAN FRANCISCO DERMATOLOGICAL ASSOCIATION

Sept. 23, 1932

C. E. SCHOFF, M.D., *in the Chair*

XEROSTOMIA. Presented by DR. H. J. TEMPLETON.

Miss B. K., aged 59, (Dr. Dorothy Allen's patient), has been annoyed for eighteen months by dryness of the mouth. During the last five months this condition has been so severe as to interfere with deglutition. No lesions are visible in the mouth except that the mucous membranes appear rather dry and atrophic. There is some gastric distress. General physical examination gave negative results, except for suggestion of sinus disease. There is no evidence of pellagra, such as dermatitis or vaginitis. A normal blood count and a high gastric acidity would seem to rule out pernicious anemia. The diet is well balanced. The blood calcium was 9.5 mg. Two hours after a meal the blood sugar was 135 mg. A culture from the mouth and stools showed the presence of Monilia; otherwise the stools were normal. The basal metabolic rate has varied from minus 20 to minus 9. Because of this low reading, thyroid extract was administered, but this failed to give relief. A roentgenogram of the chest showed normal conditions. A series of roentgenograms of the gastro-intestinal tract failed to reveal a pathologic process. The elimination of any possible local irritants, such as tooth powder, failed to give relief. As the patient has both gold and silver fillings in her teeth, I thought of Everet Lane's work. The removal of the silver fillings is being considered.

DISCUSSION

DR. H. J. TEMPLETON: This patient was presented for suggestions as to the possible etiology of the condition of the mouth and for suggestions as to therapy. I have wondered whether or not it would be worth while to remove the silver fillings in the mouth, in view of Lane's ideas, and substitute gold so that there could be no electrolytic action.

DR. MERLIN MAYNARD: Are you thoroughly convinced that she has abnormal dryness of the mouth?

DR. H. J. TEMPLETON: Absolutely. I have seen her mouth in a completely dry and glazed condition. No strong topical applications have been used which could account for her condition.

DR. H. E. MILLER: I thought that the tongue and mucous membranes of the mouth were atrophic. Considering the age of the patient, it might be a condition comparable to kraurosis vulvae. The age of the patient is compatible with such a diagnosis. In such a case, the condition is probably one for which little can be done.

DR. HOWARD MORROW: The worst case of dryness of the mouth we have seen was the result of roentgen treatment given for hypertrichosis. The dryness lasted for years. I cannot imagine what one would do in the present case, except perhaps give chlorate of potash as a mouth wash to increase the saliva.

DR. C. E. SCHOFF: I thought that the mucous membranes appeared normal, except for some dryness. What about the possibility of a neurogenic origin? We all know how public speakers are apt to have dry mouths when they are nervous. This aspect might be worth investigating. Would not potassium iodide be of value in testing the function of the salivary glands?

DR. N. N. EPSTEIN: The presence of Monilia in the mouth is common and not of etiologic significance.

MONGOLIAN SPOT. Presented by DR. L. R. TAUSSIG.

An otherwise healthy Japanese boy, 10 months of age, presents a scattered blue, macular eruption covering most of the chest and back and the outer surfaces of the arms. There are also black spots on the sclera. The usual mongolian spot was present over the coccygeal area at birth, and apparently has spread to the present extent. The Wassermann test of the blood was negative. An older brother has the normal mongolian spot of his race.

DISCUSSION

DR. L. R. TAUSSIG: Ebert, in 1927, at the April 20 meeting of the Chicago Dermatological Society, presented a Mexican child with congenital syphilis and extensive pigmentation of this type. Other children of the family had had the usual type of mongolian spot, which disappeared. At the same meeting, Oliver, Senear and Finnerud remarked that they had seen similar extensive cases.

Apparently such cases do occur, but I have never seen a description of so extensive a lesion in the literature. Mongolian spots usually clear up, of course, before the sixth or seventh years. The important practical point is whether or not we can tell this child's family that this extensive spot will clear up in the usual time.

I do not know whether or not the pigmented spots on the sclera are a part of the condition.

DR. H. E. MILLER: The older dermatologic texts will tell you that these lesions vary from a few centimeters in diameter to those that cover most of the body. They involute spontaneously as a rule before the child is 5 or 6 years of age.

DERMATITIS SOLARE. Presented by DR. H. J. TEMPLETON.

J. B., a dentist, consulted us in July, 1932, because of an erythematovesicular dermatitis of the forehead. He stated that this attack of dermatitis is only one of the many which he has had since childhood and which are always produced by exposure to sunshine.

The eruption, which is beginning tonight, is the result of experimental exposure to sunshine yesterday and today. In July, we applied suberythema doses of ultraviolet rays from two sources (one predominating in wavelengths of 3,200 angstroms and the other in wavelengths of 2,500 angstroms), but no dermatitis resulted. One half of an erythema dose of unfiltered roentgen rays likewise failed to produce an eruption. The urine will be tested for hematoporphyrin when the present attack has reached its height. We have suggested Barber's treatment consisting of a meat-free diet, dilute hydrochloric acid by mouth and a stool vaccine.

DISCUSSION

DR. H. J. TEMPLETON: Dr. B. seems to have a rather severe case of dermatitis solare. How can we so alter the reactivity of the skin as to cut down the frequency of occurrence and prevent attacks in the future?

Barber has obtained good results in some cases with meat-free diet, hydrochloric acid by mouth and a stool vaccine. We treated one patient with a meat-

free diet, hydrochloric acid and vaccine. The condition cleared up, and the patient remained well as long as the vaccine was used, but he had a relapse after it was discontinued.

DR. H. E. MILLER: I would assume that this eruption was a seborrheic dermatitis, perhaps brought out by sunshine. It occurs only on the lower part of the forehead near the brows and not on any other areas on the face that come in contact with sunshine. I suggest fractional roentgen therapy.

DR. MERLIN MAYNARD: A felt hatband might be a factor. The patient wears a hat a great deal, and the forehead is more intimately in contact with the hatband than is the central area of the head.

I see many cases of solar dermatosis in the Santa Clara valley. I have used Bacillus acidophilus with success. One patient discontinued the acidophilus, and a relapse occurred. On the resumption of acidophilus the eruption disappeared. I have not had much faith in the use of the colon bacillus in the treatment for this condition. We will probably find more Welch bacilli than those of the colon group. Administration of hydrochloric acid is the same type of therapy. It is difficult to give enough hydrochloric acid to do much good.

DR. E. K. STRATTON: I should like to see Dr. Templeton try roentgen therapy, as suggested by Dr. Miller. If the condition is a seborrheid, it will clear up. On the other hand, if it is dermatitis solare, the roentgen therapy is liable to aggravate it. I have observed that several persons who were sensitive to the actinic rays also reacted unfavorably to the roentgen rays.

DR. H. J. TEMPLETON: I am willing to accept the idea that seborrhea may play a rôle in this case, but I do not think that the seborrhea is basically responsible for the dermatitis. A patch test with the hatband will be made.

TABES DORSALIS. Presented by DR. N. N. EPSTEIN.

Mr. O. N., aged 37, whose condition had been diagnosed as tabes dorsalis, received diathermy treatments for lightning pains in the lower extremities on August 25, September 1, 8, 16, 22 and 29 and October 6 and 13. Following the fourth treatment the pains ceased and have not recurred. It was thought that it might be worth while to present a patient with tabes dorsalis with severe lightning pains. This type of pain is most difficult to control. Antisyphilitic drugs as a rule do not give relief. This patient was a caddy who came to the clinic because the ataxia interfered with his work. He was given a considerable amount of antisyphilitic treatment, without relief from the pain.

DISCUSSION

DR. H. E. MILLER: How high was the fever?

DR. N. N. EPSTEIN: The temperature gradually rose to 103 F. on the first treatment. If the patient's condition is good, the temperature may be held at this height for several hours. When the current is shut off, the temperature, instead of falling, may remain stationary or rise for two or three hours; but this can be controlled by proper measures. The nursing care is particularly important. Following the first treatment, the temperature may be allowed to rise to 105 F.

The technic is rather involved. Two electrodes are used, one on the back and one on the trunk. It takes from one to two hours to raise the temperature to the proper height. The chief dangers are: (1) the rise in temperature after the current is shut off and (2) superficial burns from the electrodes.

DR. MERLIN MAYNARD: Can you explain the rise in temperature following the shutting off of the current?

DR. N. N. EPSTEIN: It must be due to some disturbance in the temperature-regulating mechanism. That is all one can say. These patients come in one morning and are ready to go back to work the next morning. Very few patients are debilitated by the condition.

PHILADELPHIA DERMATOLOGICAL SOCIETY

J. P. GUEQUIERRE, M.D., *Secretary*

Sept. 30, 1932

J. M. SCHILDKRAUT, M.D., *Presiding*

A CASE FOR DIAGNOSIS. Presented by DR. A. STRAUSS.

P. S., a woman, aged 43, had had swelling and coldness of the hands for over twenty years, the hands and fingers being especially stiff in the morning. When she was first seen, in February, 1931, the hands were cold, red and puffy, and the fingers somewhat deformed, though she used them easily.

She had an operation on the right arm five years previously. She had abscesses of the bones in childhood. She suffered from flatulence, indigestion, pains in the middle of the chest and cardiac distress. Tonsillectomy performed seven years before had reduced the choking sensation.

The action of the heart was normal, and there was no history of paroxysmal asphyxia of the fingers. There was no progression of the condition. The skin of the dorsum was shriveled and atrophic, and the fingers were like pincushions, the region of the proximal phalanges being mainly affected. There was no report on a roentgen examination. The basal metabolic rate was slightly subnormal.

DISCUSSION

DR. S. S. GREENBAUM: I saw this patient about ten years ago. I considered the condition of the fingers trophedema.

CHANCROID OF THE RIGHT UPPER EYELID. Presented by DR. S. S. GREENBAUM.

W. H., a colored man, aged 35, presented an oval ulcer on the right upper eyelid, roughly 1 by 2 cm. in diameter. When first seen the lesion was crusted. At the time of presentation there was a superficial ulcer with undermined borders. On the right arm there was a pinhead-sized ulceration, which developed following auto-inoculation from the eyelid.

The patient also had a mixed infection on the penis (chancre-chancroid). The Kahn test was — 2 2 2. Smears and cultures from the lesion on the eyelid were negative for the Ducrey bacillus.

Great care should be taken in interpreting the auto-inoculation test. The test in this case was definitely positive. The lesion was very small; one is apt to be misled by such small positive reactions. If the crust is removed, even in these very small positive auto-inoculation tests, a minute ulceration is always found.

XANTHOMA MULTIPLEX AND PRENATAL SYPHILIS. Presented by DR. G. V. KULCHAR for DR. JOHN H. STOKES.

C. D., a Negro boy, 7 years of age, was presented at the April meeting of the society, at which time there were numerous xanthomatous nodules of one month's duration over the wrists, elbows, trunk, buttocks and thighs. In addition, there were xanthomatous striae over the palms. Biopsy confirmed the diagnosis of xanthoma multiplex. The blood cholesterol was 379 mg. per hundred cubic centimeters, and the blood sugar, 112 mg. There had been a gradual involution of the lesions until, at the time of presentation few remained. The patient had been given antisyphilitic treatment because of a prenatal infection.

DYSTROPHY OF THE NAILS. Presented by DR. E. F. CORSON.

E. S., a woman, aged 22, single. presented dystrophy of all the nails except those of the fourth and fifth toes on both feet. The condition had begun two years

previously on the right thumb, and then involved the left thumb, the right fingers, the left fingers and some of the toes a year later. The patient attributed the onset to nervousness and a "run down" condition at that time; there had been no illness, accident, operation or nervous shock.

DISCUSSION

DR. E. F. CORSON: This girl reminded me very much of a patient whom Dr. Pfahler showed last winter whose condition evoked discussion as to whether it was a fungus infection or some trophic change. I feel that the curious symmetrical distribution and the mode of onset suggest a systemic background, but what it is is not apparent. I think that apart from fungus infections and as parts of generalized cutaneous conditions, such as psoriasis, diseases of the nails are very puzzling. The average textbook gives very little help either in differentiating them or in suggesting adequate treatment.

DR. W. O. ROOP: This young woman is a typist, and I should like to offer the suggestion of trophoneurosis of traumatic origin.

DR. JOHN H. STOKES: I believe that the diagnosis is psoriasis.

ACUTE SYPHILITIC IRITIS AND LUPUS ERYTHEMATOSUS OF THE SCALP. Presented by DR. G. V. KULCHAR for DR. JOHN H. STOKES.

A Negress, B. P., aged 39, presented an acute bilateral iritis, presumably of syphilitic origin. There was an area of alopecia with a dull erythematous border over the left temple and parietal region. Within the area there were marked atrophic scarring and numerous typical follicular plugs. The remainder of the scalp was normal.

The process was of eight months' duration, beginning as a patch of alopecia above the left ear and extending peripherally. The Wassermann reaction of the blood was strongly positive, and the patient had received two injections of bismarsen.

DISCUSSION

DR. JOHN H. STOKES: My staff made a diagnosis of lupus erythematosus, but I wonder whether one can support such a diagnosis. I wonder whether she had not had infiltrated syphilis of the scalp that destroyed the hair follicles. Those large patches are not suggestive of lupus. The left ear shows a little follicular plugging, but with what light I had I could not convince myself that it was a follicular lupus erythematosus of the scalp. It might be that some feature in the treatment rules out syphilis entirely.

DR. D. M. PILLSBURY: I believe that the process has shown definite involution since she first was seen. When we first examined her there was a slight degree of erythema and definite follicular plugging of the type now present in the left ear, but I do not know whether the bismarsen has affected the syphilitic condition or whether it had a nonspecific effect on the lupus erythematosis. I examined a patient of Dr. Greenbaum's who had a peculiar pitted scarring toward the center of the lesion and also a remarkable regrowth of hair in some of the lesions.

A CASE FOR DIAGNOSIS: ICHTHYOSIS, HYPOTHYROIDISM OR ACRODERMATITIS CHRONICA ATROPHICANS (?). Presented by DR. G. V. KULCHAR for DR. JOHN H. STOKES.

B. P., a Negress, aged 25, presented a dry, exfoliating dermatosis over the hands, feet, anterior surface of the knees, thighs and chest. The eruption was noninflammatory and the borders well defined. The Wassermann reaction of the blood was positive. The basal metabolic rate was minus 6.

The patient had been under treatment for syphilis irregularly since 1928, but had received no arsphenamine after June, 1929. In June, 1932, there was a swelling over the dorsa of the fingers and toes which subsided in about two weeks, leaving the skin of those regions loose and wrinkled. About a month following

the subsidence of the edema, a dry, exfoliative eruption appeared over the hands and feet and extended up to the wrists and ankles. About the same time, a similar eruption appeared over the anterior surface of the chest, knees, and thighs, being sharply limited to the area of garter pressure. There were no subjective symptoms. The only constitutional symptom was lassitude.

DISCUSSION

DR. C. W. WRIGHT: I disagree with the diagnosis of acrodermatitis chronica atrophicans. I think that the whole picture could be fitted in with ichthyosis.

DR. S. S. GREENBAUM: I disagree with the diagnosis suggested in this case. I think that she has an acquired symmetrical hyperkeratosis, internal in its origin, as it is on both upper and lower extremities. I do not agree with the diagnosis either of acrodermatitis or of ichthyosis.

DR. JOHN H. STOKES: I am inclined to regard the condition as a hypothyroid manifestation. I have seen this condition in patients who have not even shown a gain in weight such as this girl has shown, and I have seen a prompt response to treatment with thyroid, without recurrence. The palms are rather suggestive of ichthyosis, but there is not much to suggest acrodermatitis, such as translucence, erythema, a sort of edema or visibility of veins through the skin. I should be inclined to give thyroid and see what happens. The pleatlike folds over the shin are particularly suggestive.

PSEUDOPELADE. Presented by DR. G. V. KULCHAR for DR. JOHN H. STOKES.

D. S., a white woman, aged 45, presented irregular patches of cicatricial alopecia over the frontoparietal region of the scalp. The borders were dully erythematous. Within the patch of alopecia there were a number of normal-appearing hairs, which on epilation showed the typical glassy sheen described in connection with pseudopelade. In addition, there was asymptomatic syphilis of the central nervous system.

The Wassermann test of the blood was negative. Examination of the spinal fluid showed 63 cells. The Kolmer reaction was plus 4; the Kahn reaction, plus 4; the globulin test, plus 4, and the colloidal mastic test, 454321000.

The onset of the cicatricial alopecia was indefinite, but the condition was first noticed when the patient was about 16 years of age; it began with a small patch in the frontal region and extended to the parietal region during the course of several years. There had been no noticeable progression in the past ten years. No local treatment had been given.

DISCUSSION

DR. S. S. GREENBAUM: The patient states that she has had the condition since the age of 3. It looks like an ordinary scar.

DR. JOHN H. STOKES: There is also a good deal of alopecia over the right frontal region. The patch is not quite so definitely defined; it looks like the masculine type of alopecia, which is occasionally seen in women. However, I do not see why pseudopelade may not be present.

CHRONIC PSORIASIS, ARSENICAL HYPERPIGMENTATION, HYPERKERATOSIS, PROBABLE ARSENICAL HEPATITIS. Presented by DR. BEERMAN for DR. JOHN H. STOKES.

D. L., a white man, aged 46, was a poorly nourished man with marked abdominal enlargement (fluid) and edema of the ankles. On the skin there were palmar and plantar keratosis, marked pigmentation and a general scattering of the lesions of psoriasis. The patient had noticed abdominal swelling in July, 1932, which was followed by swelling of the feet. Previous medical history revealed only a dry pleurisy eleven years previously, and no abdominal operations. Generally, the patient had no systemic complaints beyond pain in the lower part of

the abdomen. The hyperpigmentation of the skin was of one year's duration. The patient had had psoriasis for twenty years. He stated that he did not use alcoholic beverages.

For the treatment of psoriasis the patient had received roentgen therapy and treatments with chrysarobin and ultraviolet rays. For the past three years he had received a half-strength solution of potassium arsenite, 24 drops daily, except for a cessation of from three to four weeks every two or three months.

The blood count showed: red cells, 4,240,000; white cells, from 3,700 to 6,500; hemoglobin, 78 per cent, and eosinophils, 5 per cent. Urinalysis gave repeatedly negative results. The blood urea nitrogen was 24 mg. per hundred cubic centimeters; the blood sugar, 103 mg. The tolerance for sugar was normal. The Wassermann reaction of the blood was repeatedly negative. Gastric analysis gave negative results. The result of the phenolsulphonphthalein test was 40 per cent in two hours. Fluid from the abdomen was sterile. A test for liver function showed 3 per cent of the dye in the blood after one-half hour. The eyegrounds were normal.

DISCUSSION

Dr. C. S. Wright: This patient tells me that I gave him a prescription for solution of potassium arsenite four years ago. Whether or not I marked it "Not to be refilled," I do not know. This illustrates the danger of giving a person a prescription for solution of potassium arsenite when one is unable to keep a watch on him. Instead of taking 24 drops daily he has taken only 12, for we prescribe solution of potassium arsenite diluted half-strength with cinnamon water. This is a good illustration of how patients will take medicine without advice over a long period.

Dr. S. S. Greenbaum: What did the internists find?

Dr. John H. Stokes: That is guesswork. The liver is obviously involved.

Dr. V. C. Garner: After the abdomen has been tapped, the liver is palpable and markedly enlarged, and in a cursory glance through the literature I was able to find no cases of hepatitis following so quickly after the administration of solution of potassium arsenite. It was suggested that the patient should be given sodium thiosulphate. He has received about twenty-four injections, with some benefit. The ascites has grandually been diminishing, and the abdomen has to be tapped only once in two weeks now.

A Case Presented for an Opinion as to the Best Method of Therapy. Dr. V. C. Garner.

E. W., a white man, aged 37, presented a split pea-sized, reticulated, pigmentary macule on the vermilion border of the lower lip near the midline; it was entirely asymptomatic. There was no associated adenopathy. It was of slow growth, from six months to one year in duration. The patient was formerly a heavy smoker, but he has not smoked in the two months prior to presentation.

DISCUSSION

Dr. W. O. Roop: The lesion apparently is benign, and very slightly disfiguring. I should let the lesion alone. If the patient insisted on treatment I should probably suggest the use of a caustic like trichloracetic acid, which is easily controlled and could be repeated, or, possibly, I should try electrodesiccation. But I believe that any method of treatment would probably produce a more unsightly condition than is now present.

Dr. John H. Stokes: I do not like pigmented macules on the lips, and I should exercise this one with high frequency cautery, cutting deeply.

Dr. S. S. Greenbaum: I was wondering how frequently one sees a melanoma of the lip. I have seen a number of such growths, which I term acquired pigmented nevi of the lip, and I have always advised letting them alone. I do not recall reading in the recent literature of melanomas developing in them.

DR. V. C. GARNER: I was constrained to present this patient on account of a similar case presented in New York, where I was amazed by the great diversity of opinions suggested by the members for the treatment of a lesion of this type. Before I came to a definite decision, I was anxious to get your opinion as to how you would treat the condition. The lesion is of only a year's duration. The patient has given up smoking. He does not insist on any treatment, except that which will preserve his health and life.

DR. JOHN H. STOKES: As Dr. Greenbaum has said, I have not seen any of these lesions eventuate in melanomas, but then how many nevi one sees that do not eventuate in such a way. However, when a lesion develops into a melanoma, one fervently wishes that one had removed it.

DR. C. S. WRIGHT: I think that the cure of the patient's mental condition is worth something. Patients worry about such a lesion the rest of their lives. I believe in removing such a growth by electrodesiccation.

INFECTIOUS GRANULOMA WITH PROBABLY BEGINNING NEOPLASTIC PROPERTIES. Presented by DR. H. U. NORTH.

M. G., a man, aged 46, from the Skin and Cancer Hospital, had noticed a reddish papule on the left leg three years previously. This lesion steadily increased until it measured about 12 sq. cm. At the time of presentation the lesion was infiltrated, plaquelike, sharply circumscribed, purplish and slightly scaly. There were no subjective symptoms other than occasional light itching.

Biopsy showed slight dilatation and proliferation of the capillaries of the corium and some hemorrhage into the surrounding tissues; the corpuscles did not take the stain well, but they could be seen as transparent round cells. There were proliferation of the endothelium and a perivascular proliferation of spindle and round cells and pigmentation. Except for the small amount of hemorrhage into the tissues, this is the histologic picture of Kaposi's multiple hemorrhagic sarcoma.

DISCUSSION

DR. H. U. NORTH: The fact that impressed me about this case is that it conforms so closely to the picture of Kaposi's multiple hemorrhagic sarcoma. There are hemorrhage in the tissues, a large number of round cells, perivascular proliferation of the capillaries and the usual distribution of pigment. The lesion is of three years' duration, and there is another one forming on one side of it. There is only occasional mild itching.

DR. JOHN H. STOKES: I do not feel that I can make a diagnosis. I had one case in Philadelphia in which carcinoma developed. I have seen six other cases in which carcinoma did not develop. I was impressed at once by the basal configuration of the lesion. The condition does not suggest to me Kaposi's multiple hemorrhagic sarcoma. The patient has a marked vascular disturbance of the leg; I do not see why periodic hemorrhages of his skin should not occur. I must confess that I could not diagnose the pathologic condition.

SCLEREMA NEONATORUM. Presented by DR. S. S. GREENBAUM.

A colored infant 3 weeks old presented four or five indurated areas on the trunk and upper limbs. The extent of the induration varied, but there was no pitting on pressure. The Kahn test was negative.

DISCUSSION

DR. JOHN H. STOKES: We used to administer inunctions in such cases regardless of the serologic observations.

MINNESOTA DERMATOLOGICAL SOCIETY

D. D. TURNACLIFF, M.D., *Secretary*

Oct. 5, 1932

H. N. KLEIN, M.D., *President, Presiding*

IDIOPATHIC MACULAR ATROPHY. Presented by DR. H. N. KLEIN, St. Paul.

The patient, a man, first had the condition in June, 1931, when it began with the appearance of white spots about the size of a dime on the anterior side of the neck, in the midline, just above the sternoclavicular articulation. Subsequently many other spots appeared, varying in size from that of a split pea to that of a quarter. There was no itching, but all the lesions were distinctly atrophic. (A biopsy by Dr. John F. Madden confirmed the diagnosis.)

DISCUSSION

DR. HAMILTON MONTGOMERY, Rochester: I believe that the diagnosis should be lichen sclerosus et atrophicus of Hallopeau. There are numerous keratotic plugs in the center of the lesions.

DR. L. H. WINER, Minneapolis: From the biopsy alone, one could believe the condition to be a healing, idiopathic atrophy. One can see there is atrophy clinically, as well as microscopically. There are hyperkeratotic plugs in each follicle in the individual, more recent lesions. Lichen sclerosus as the diagnosis can be admitted.

PSEUDOXANTHOMA ELASTICUM. Presented by DR. S. E. SWEITZER, Minneapolis.

The patient, L. O., aged 14 years, complained of an eruption which had been present for nine months, limited to the dorsa of the hands and the flexor and extensor surfaces of the arms to the shoulders. It began on the knuckles of the hands as elevated, white, infiltrated, firm papules, the size of a split pea. In the course of three months the lesions had ascended to the wrists, and in the course of nine months had reached the shoulders. There had been no subjective symptoms at any time. The lesions on the arms above the wrists were mostly the size of a pinhead and most numerous on the flexor surfaces. The past history was essentially negative. The patient had had no serious illnesses, but was born with strabismus. His mother had died of smallpox; his father was living and well.

Examination showed a well developed boy, aged 14 years. On the dorsa of the hands and fingers were hundreds of achromatic, firm, indurated papules varying in size from that of a pinhead to that of a pea. The palms were absolutely free from eruption. The lesions were most numerous over the metatarsophalangeal joints and over the styloid processes of the radii. There were a few lesions on the extensor surfaces of the forearms, but they were most numerous on the flexor surfaces. They were equally numerous on both arms, although there were fewer lesions above the elbows. Histologic sections were shown.

DISCUSSION

DR. S. E. SWEITZER, Minneapolis: This condition is extremely rare. When I first saw the patient, I thought of degeneration of amyloid. This the biopsy, however, failed to show, but it did show degeneration of the collagen. Pseudoxanthoma elasticum occurs more often in the female, and the patients are usually much older than this boy, although a few cases have been seen in young subjects. The location in this instance is unusual. The backs of the fingers and hand, and the forearms are involved. The neck is free; most of the cases described show involvement of the neck. There was no hereditary influence. Often there is a

history of several instances in one family. This was an interesting case; I could not remember having seen a similar one.

DR. HAMILTON MONTGOMERY, Rochester: There is nothing in the section to warrant a diagnosis of colloid milium or amyloid degeneration of the skin, although clinically these would seem to be the most likely possibilities. It is true that the sections show degeneration of the collagen fibers, but this is a diffuse process and resembles that seen when the biopsy material has been left too long in the paraffin bath. I note that one of the two specimens for biopsy was taken from the knuckle, which is far from being a good site, as it is an area that is subject to a great many histologic changes resulting from too long a period in the paraffin bath.

DR. PAUL O'LEARY, Rochester: Has lichen nitidus been eliminated?

DR. H. E. MICHELSON, Minneapolis: I feel sure that the condition is not that of amyloidosis. Also, in answer to Dr. O'Leary, it is not lichen nitidus, either clinically or microscopically, for that is a condition which can be definitely diagnosed with the aid of the microscope. I think that the case may be placed, clinically, under the general heading of collagenous degeneration, but differential staining and careful observation will be necessary to enable one to arrive at a definite decision. I think that the condition clinically answers the description of pseudoxanthoma elasticum, and I recommend that the retina be examined for angioid streaks, a condition which has been described as an accompaniment or as part of the syndrome in pseudoxanthoma elasticum.

DR. HAMILTON MONTGOMERY, Rochester: I agree that there is no histologic evidence of lichen nitidus. The diffuse change seen in the connective tissues in this case can be duplicated in sections of normal skin that are left in the paraffin oven too long, with a resultant edema and loss of staining properties of the collagen fibers.

DR. L. H. WINER, Minneapolis: Biopsy of one of the lesions shows a marked hyperkeratosis of the epidermis, but no other changes. The papillary cutis shows no changes. The lower reticularis shows the collagen irregularly grouped and bundles of connective tissue fragmented. The elastic tissue in these areas (Weigert's stain) is split and fragmented.

DR. S. E. SWEITZER, Minneapolis: Lichen nitidus had been eliminated. The reason a biopsy was not taken from the arm was that the patient had such extensive lesions on the hand, and, at that time, such limited involvement of the arm that no one would have thought of taking a specimen for biopsy from it. Two biopsies have now been made.

LICHEN SYPHILITICUS. Presented by DR. S. E. SWEITZER, Minneapolis.

J. B., aged 27, stated that he was exposed to syphilis eight weeks before presentation. Two weeks after exposure a lesion appeared on the penis, which healed in about five days. Almost directly after the healing of this lesion a generalized macular eruption appeared, and in another week it became papular and had remained so for the past three or four weeks.

Examination showed a healed lesion on the shaft of the penis. There was also a generalized follicular eruption made up of dull red papules, with no special localization, varying in size from that of a pinhead to that of a split pea. The extensor surfaces of the arm, the face and the back were most intensely involved. Many of the papules were capped with a slight scale, the lesions resembling pinpoint psoriasis. There were no lesions of the mucous membrane. The Wassermann and Kahn tests were positive.

PAPULONECROTIC TUBERCULID. Presented by DR. JOHN F. MADDEN, St. Paul.

This and the following cases are from the department of dermatology and syphilology of the Ancker Hospital, St. Paul, services of Drs. Klein and Madden. Madden.

Mrs. C. R., a housewife, aged 45, stated that the present eruption appeared in December, 1931. After that the lesions were present constantly. She presented an eruption confined to the extensor surfaces of the elbows and to both ears. This appeared as inflamed, painful, dull red papules, varying in size from that of a pinhead to that of a pea, which necrosed in the center, sloughed and left atrophic scars. The ears appeared "motheaten." The lesions were in all stages of evolution and involution. Roentgen pictures of the chest were negative. The family history was negative. The Mantoux test was strongly positive; the Wassermann test of the blood was negative. Biopsy was compatible with papulonecrotic tuberculid.

DISCUSSION

DR. JOHN BUTLER, Minneapolis: I think that the condition is a nodular syphilid.

DR. F. R. WRIGHT, Minneapolis: I thought that the condition was syphilis, but there is no infiltration of the skin, and there ought to be in syphilis or tuberculosis.

DR. JOHN F. MADDEN, St. Paul: I am going to treat the patient with small doses of neoarsphenamine. This will be of no diagnostic help, however, because both syphilis and papulonecrotic tuberculid can respond favorably to arsenic.

DR. HAMILTON MONTGOMERY, Rochester: The histologic sections show a nonspecific type of perivascular infiltrate which, however, is not inconsistent with the early changes seen in any type of hematogenous tuberculosis. There was nothing to suggest a syphilitic process in the pathologic picture.

DR. JOHN F. MADDEN, St. Paul: I think the findings are in favor of the diagnosis of papulonecrotic tuberculid. The focus of infection could not be found, but that is not unusual.

TERTIARY SYPHILIS: JUXTA-ARTICULAR NODULES ASSOCIATED WITH MULTIPLE NODULO-ULCERATIVE LESIONS. Presented by DR. JOHN F. MADDEN, St. Paul.

Mrs. W. N., a housemaid, aged 57, stated that ulcers appeared on the anterior surface and proximal third region of both legs about fifteen years before presentation. As the older lesions healed, new ones had appeared constantly since that time. She had no treatment until April, 1932, when she was given injections of 2 grains (0.13 Gm.) each of bismuth salicylate in oil. The patient stated that the ulcers healed at that time, and that no activity was noticed until approximately six months later. The eruption had been painless, and would have gone untreated had it not been discovered while the patient was being examined for other complaints. She presented an eruption extending from the distal third of the thighs to the middle third of the legs, which was more marked on the anterior surfaces. There was atrophic scarring, associated with discrete and confluent, dime-sized, dully inflammatory nodules and ulcers. The scarring and active lesions exhibited a polycyclic border. There were subcutaneous, freely movable, painless nodules, varying in size from that of a bean to that of an olive, about the anterior and lateral surfaces of the knee joints. The Wassermann test of the blood was 4 plus. A specimen taken from a node for biopsy showed nonspecific inflammation.

DISCUSSION

DR. PAUL O'LEARY, Rochester: This case calls attention to the fact, recently emphasized in the literature, that all so-called juxta-articular nodes in a syphilitic patient do not involute with treatment. Fibrous nodules such as this patient presents are but little influenced by treatment of the syphilis; accordingly, prognostications should be reserved until a thorough course of treatment has been completed.

DR. HAMILTON MONTGOMERY, Rochester: It is interesting to note that the histopathologic changes in juxta-articular nodes due to syphilis do not present the histopathologic features of the disease, although they respond promptly to antisyphilitic treatment, as a rule.

ACNE VARIOLIFORMIS. Presented by DR. JOHN F. MADDEN, St. Paul.

J. S., a Negro, aged 59, had had a pruritic eruption confined to his scalp and face for three years before presentation. The lesions were more numerous on the forehead about the margin of the hair. The patient first noticed a stinging sensation, followed in a few hours by an inflammatory papule the size of a glass pinhead. The center of the papule became necrotic, sloughed and left a pitted scar. All stages of the eruption were present. Biopsy was compatible with a diagnosis of acne varioliformis. Roentgenograms showed no signs of pulmonary tuberculosis.

THROMBO-ANGIITIS OBLITERANS. Presented by DR. JOHN F. MADDEN, St. Paul.

Mrs. A. J., a Polish housewife, aged 26, consulted a doctor because of pain in both legs. The pain interfered with her housework and kept her awake at night. She had first noticed pain, redness and swelling in her feet about two years before presentation. Since that time the pain had been progressive, and the redness and swelling had extended to the upper third part of the legs. Both legs showed definite change in temperature, and were cold to a spot about an inch (2.5 cm.) below the knees. There were two superficial veins on each leg, one above and one below the knee, which showed evidence of a recent thrombophlebitis. The dorsalis pedis arteries were palpable.

A general examination gave negative results. Roentgenograms of the legs and urinalysis gave negative results. Red blood cells numbered 3,940,000, and the white cells, 7,000, and hemoglobin was 72 per cent. The chemical examination of the blood showed it to be normal. A differential blood count showed: polymorphonuclear neutrophils, 59 per cent; lymphocytes, 34 per cent; monocytes, 5 per cent, and eosinophils, 2 per cent. The Wassermann test of the blood was negative.

DISCUSSION

DR. PAUL O'LEARY, Rochester: This is a most unusual case, particularly if further observation confirms the diagnosis of thrombo-angiitis obliterans. This is an exceptionally rare disease in women, the ratio being about one case in the female to one hundred in the male. The fact that the patient says that she has no pain in the foot on walking, but mentions discomfort in the calf, which has a tendency to involve the right leg only, are points against the diagnosis of thrombo-angiitis obliterans. On the other hand, the inability to feel the pulsations of the dorsalis pedis artery, the rubra of the right foot and the progressive phlebitis are features in favor of the diagnosis. This case emphasizes another point, namely, the need for utilizing the differential diagnostic procedures recently developed for the recognition of the vascular diseases of the extremities. I refer to the estimation of the vasomotor index and roentgen examination of the extremities with the aid of a colloidal thorium dioxide preparation. If these procedures are not available, a therapeutic test of repeated intravenous injections of typhoid vaccine in conjunction with the constant wearing of a heavy rubber bandage, not an elastic stocking, might readily eliminate the possibilities of a recurring and progressive thrombophlebitis as the cause of the patient's difficulty. Raynaud's disease is easily eliminated, because the history shows absence of changes of color in the fingers, and the fact that exposure to cold does not aggravate the condition.

DR. JOHN F. MADDEN, St. Paul: The patient told me an entirely different story. She came to the dispensary two days ago seeking relief from pain. I shall start the treatment that Dr. O'Leary suggests as soon as the proper bandage can be obtained.

PSEUDO-EPITHELIOMATOUS HYPERPLASIA (OF WHITE AND WEIDMAN) AT THE BORDER OF A STASIC ULCER. Presented by DR. JOHN F. MADDEN, St. Paul.

Mr. F. O., a carpenter, aged 58, had had more or less edema of the feet since he was 20 years of age. During the winter of 1910 his feet were frozen. Both legs became edematous, and a large ulcer appeared on the left leg, which healed. Both legs were edematous after that. Since 1913 one leg or the other would ulcerate about every two years. The patient would retire to a hospital until the ulcer healed with rest in bed and wet packs. The ulcer under consideration appeared on the right leg about four months before this presentation. The patient was admitted to my service in August, 1932, with a foul ulcer covering the anterior and most of the lateral surfaces of the lower third and half of the middle third portions of the right leg. The border was shelving and showed marked hypertrophy. The base was covered with a foul crust and purulent discharge. There was an associated edema of both legs. About eight weeks later, in October, 1932, the border had flattened out, and the ulcer had healed, except for a thin, pencil-like central portion.

The patient's treatment consisted of rest in bed, elevation of the leg, wet dressings of surgical solution of chlorinated soda and a light cradle. There was no inguinal adenitis. The border of the former ulcer was freely movable. There was no gross infiltration of tissue. The Wassermann test of the blood was negative. The diagnosis on biopsy by every one who saw the section was squamous cell carcinoma.

DISCUSSION

DR. HAMILTON MONTGOMERY, Rochester: The histopathologic changes in a pseudo-epitheliomatous hyperplasia, as Dr. Madden has stated, have been thoroughly discussed in an article by Drs. Weidman and White. I have had several cases in which confusion with epithelioma has arisen, especially two cases of bromoderma and several of indolent tertiary syphilids. In these lesions there may be a marked irregular acanthosis, with irregular pearl formation and considerable inflammatory reaction in the connective tissue at the advancing borders of the process. Unlike epithelioma, however, there are relatively few mitotic figures to be found, and the infiltrate in the cutis can be seen invading the acanthotic epidermis, resulting in considerable destruction. The advancing margins of the epithelioma, on the contrary, show numerous mitotic figures, and in the lower grades of malignancy are sharply defined from the infiltrate beneath.

FIBROMA MOLLUSCUM GRAVIDARUM AND VON RECKLINGHAUSEN'S DISEASE. Presented by DR. JOHN F. MADDEN, St. Paul.

Mrs. G. H., a housewife, aged 35, was referred from the prenatal clinic because of many tumors on the skin. She stated that the nodules had appeared during the second or third month of her four pregnancies. The lesions reached a certain size and remained stationary until about two months post partum, when they all disappeared. She said that the large tumors on the right shoulder and nipple remained permanently. The eruption consisted of many soft, brown, painless nodules, pedunculated and sessile, varying in size from that of a pea to that of an olive and spread over the entire cutaneous surface, but more markedly on the trunk. There were two larger lesions of the same type: one on the right shoulder, the size of an egg, and one on the left nipple, the size of a large olive. The patient was five months pregnant. Urinalysis gave negative results. The Wassermann test of the blood was negative.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: I think that this is a case of von Recklinghausen's disease because of the large, fixed tumors, especially those on the shoulder and the right nipple. The cases of fibroma molluscum gravidarum that I have seen showed many small, pedunculated lesions. They were mere tags of tissue present in the axillae and on the sides of the neck. Sometimes all the lesions disappeared after the period of gestation, and at other times some of

the lesions remained and had to be removed with the cautery. I have also seen this type of pedunculated fibroma as an accompaniment of adenoma sebaceum.

DR. JOHN F. MADDEN, St. Paul: Dr. Ormsby, in his text, describes fibroma molluscum gravidarum under the general heading of von Recklinghausen's disease.

Brickner's original description of the disease is that of an unusual form of von Recklinghausen's disease developing in women during pregnancy and subsequently disappearing. I shall test the patient's veracity by keeping her under observation and try to show her at another meeting.

TRICHOPHYTOSIS. Presented by DR. JOHN F. MADDEN, St. Paul.

Mr. C. E., a student, aged 25, presented a small, orange-sized lesion on the extensor surface of the left wrist and a similar lesion located on the lower third of the left leg. Both lesions started as small papules about six months previous to presentation. They had spread peripherally and become less active in the central portions. The border was made up of inflammatory pustules the size of a pinhead, some of which were covered by a crust. The signs of activity decreased as the center of the lesions was reached. An ectothrix was found in fresh preparations.

DISCUSSION

DR. D. D. TURNACLIFF, Minneapolis: I recently had the opportunity to try out Dr. Kingery's mixture of oils of thyme and cinnamon in gutta percha on the scalp. In my case a folliculitis started at the end of about five days. This has cleared up; since then I have not been able to find any fungi. Dr. Kingery's prescription is: 1 per cent oil of thyme, 0.5 per cent oil of cinnamon, 10 per cent lead carbonate and 10 per cent gutta percha in chloroform. The details are given in an article in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY (**20**:797 [Dec.] 1929).

DR. JOHN BUTLER, Minneapolis: Was not the lesion a kerion? What was the causative fungus?

DR. D. D. TURNACLIFF, Minneapolis: No, but the reaction produced was equivalent to a kerion as far as therapeutic result is concerned.

A CASE FOR DIAGNOSIS. Presented by DR. JOHN F. MADDEN, St. Paul.

Mr. F. O., a retired laborer, aged 67, presented a generalized eruption of one year's duration. The legs, arms, neck and trunk were involved in the order given. There was no seasonal variation. The eruption was intensely pruritic. The lesions were irregular patches and plaques, varying in size from that of a dime to that of a quarter, which seemed to spread peripherally and increase in thickness. They tended to remain discrete. All the lesions were deep, reddish blue. Some of the plaques were made up of closely packed vesicles and vesicopustules and were covered by a crust. The Wassermann test of the blood was negative. The hemoglobin was 72 per cent; the red blood cells, 4,100,000, and the white, 5,300. A differential blood count showed: polymorphonuclears, 56 per cent; lymphocytes, 24 per cent; monocytes, 13 per cent, and eosinophils, 7 per cent. A biopsy specimen was shown.

DISCUSSION

DR. JOHN BUTLER, Minneapolis: How long has this condition been present?

DR. JOHN F. MADDEN, St. Paul: About a year.

DR. JOHN BUTLER, Minneapolis: The amount of itching and the grouping of the lesions suggest Duhring's disease.

DR. PAUL O'LEARY, Rochester: In the differential diagnosis I considered a lymphoblastomatous disease, probably mycosis fungoides, as the first choice, with an eczematoid process as the second possibility. Several of the plaques were definitely infiltrated. In a man, aged 67, the lymphoblastomas are frequently atypical and run a benign and slower course.

DR. HAMILTON MONTGOMERY, Rochester: The histopathologic picture in this case is strongly suggestive of mycosis fungoides. There is no spongiosus or any

other feature to suggest eczema or an allergic type of dermatitis. On the other hand, there is definite histologic evidence of scratch papules and of an infiltrate composed of a multiplicity of cell types with considerable pyknosis and karyorrhexis of the individual cells, and some clumping of the cells.

DR. H. N. KLEIN, St. Paul: The lesions vary in color, and this may be of some significance; the condition is suggestive of an early mycosis fungoides. Professor Kren of Vienna mentions this symptom as a prominent feature of the premycotic stage.

CHRONIC DISCOID LUPUS ERYTHEMATOSUS: RESULTS OF TREATMENT WITH BISMUTH. Presented by DR. JOHN F. MADDEN, St. Paul.

Mr. O. S., a laborer, aged 54, stated that the present eruption began about twenty-two years before presentation. After that it gradually increased until most of the face was involved. The patient had had various types of treatment, with no beneficial results. He presented an atrophic scar covering both cheeks above the line of the mouth, the nose, most of the forehead and the anterior portion of the scalp. He received seventeen injections of 2 grains (0.13 Gm.) each of bismuth salicylate in oil from January to April, 1932. He received no treatment after that, and the eruption did not recur.

DISCUSSION

DR. H. N. KLEIN, St. Paul: Was therapy with gold compounds tried in this case?

DR. JOHN F. MADDEN, St. Paul: No.

DR. D. D. TURNACLIFF, Minneapolis: I recently used bismuth in a case of lichen planus, with good results. I also used it in several cases of verruca vulgaris (after a report in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY [**26:1** (July) 1932]), with no success.

DETROIT DERMATOLOGICAL SOCIETY

H. J. PARKHURST, M.D., *Reporter*

EMMETT C. TROXELL, M.D., *Presiding*

Regular Meeting, Oct. 18, 1932

DYSTROPHY OF THE NAILS. Presented by DR. CLAUD W. BEHN and DR. JOHN H. BESANCON.

M. N. a well developed, healthy boy of 13 years, stated that about eighteen months prior to this presentation the nails of his fingers and toes became rough, markedly thinned and very friable. All of the nails were involved simultaneously. The condition was persistent, with occasional intervals of apparent improvement. There were no other ectodermal abnormalities.

The patient had six brothers and sisters, all healthy, and none of them presented a similar condition. The Wassermann reaction was negative. The basal metabolic rate was —17. The calcium content of the blood was 10.8 mg. per hundred cubic centimeters, and the phosphorus content, 3.6 mg.

DISCUSSION

DR. WILLIAM G. WANDER: One year ago I presented a girl, aged 5 years, whose nails had been hypertrophic since birth and in whom the condition cleared up under endocrine therapy.

DR. GEORGE VAN RHEE: The condition may clear up under treatment with thyroid.

LICHEN PLANUS INVOLVING THE NAILS. Presented by DR. HOWARD J. PARKHURST.

H. G. P., a physician, aged 47, had stubborn pruritus ani several months before this presentation. There were no visible lesions. The pruritus finally subsided after roentgen irradiation. In June, 1932, following a mild outbreak of herpes progenitalis, typical lichen planus lesions appeared on the penis, forearms, hands and legs, lips and buccal mucosa, accompanied by moderately severe paronychia, affecting all of the fingers of both hands simultaneously. Deformities of the nails appeared, and with a course of injections of mercuric salicylarsenate the eruption gradually disappeared, except for a medium coin-sized thickened patch on the leg and small papules on the ankles and dorsa of the feet.

At the time of presentation the nail beds did not seem to be inflamed. All of the finger-nails presented rather deep transverse furrows and a reedy dryness, and

Lichen planus involving the nails.

all were affected at the same point. Several toe-nails appeared friable, but not all, and the possibility of dermatophytosis could not be excluded. No irradiation had been employed.

NOTE.—One month later all of the toe-nails were found to be transversely furrowed, the condition being similar to that of the finger-nails.

DISCUSSION

DR. GEORGE H. BELOTE: The change in the nails may be the result of any inflammatory process, but it may be due to lichen planus.

DR. LOREN W. SHAFFER: The involvement of the toe-nails may be the same as that of the finger-nails.

DR. ROBERT C. JAMIESON: Recently I saw a similar disturbance involving the nails in a young woman who was on a diet low in vitamins.

HYPERPIGMENTATION DUE TO PERFUME. Presented by DR. HOWARD J. PARKHURST.

Mrs. H. P., aged 37, presents a sharply outlined dark brown patch, about 2 cm. long and 0.5 cm. wide, on the side of the neck below each ear. These patches appeared without noticeable erythema three days prior to this presentation, a day or two after the application of a new perfume and exposure to intense sunlight. The name of the perfume could not be ascertained. A variety of perfumes had been used on other occasions, but had never produced a similar effect.

DISCUSSION

DR. EMMETT C. TROXELL: Early last summer I saw a similar case, but the inflammatory element was outstanding.

DR. HOWARD J. PARKHURST: I have had two previous cases, in both of which the inflammatory element was prominent.

A CASE FOR DIAGNOSIS. Presented by DR. B. H. LARSSON (by invitation).

M. R., an Italian girl, aged 18, stated that late in June, 1932, she first observed a small "pimple" on the right side of her nose. It gradually enlarged, covering the right side of her face, without any pain or discomfort. The general health was good.

On examination, a sharply outlined, raised, erythematous, indurated area extended from the lower eyelid to the upper lip, and from the nose laterally to a point beyond the malar eminence. It was mobile and painless. On the side of the nose there was a necrotic, crater-like ulcer, about 1 cm. in diameter, with punched-out borders. Nothing abnormal was found in the nose or throat, and the teeth were in good condition. The pulse rate was 100, and the temperature, 100.4 F. There was no glycosuria or albuminuria, and the Wassermann and Kahn reactions of the blood were negative. Gradual improvement followed the administration of a few doses of stock acne vaccine. A considerable general reaction followed two intramuscular injections of milk.

Microscopic examination showed a chronic inflammatory process and no tubercles.

DISCUSSION

DR. ANDREW P. BIDDLE: There is too much infiltration for lupus erythematosus, and there has been too rapid development for lupus vulgaris. The condition may be facticious.

DR. LOREN W. SHAFFER: In the diagnosis an acute infectious reaction, granuloma or a malignant process must be considered. The diagnosis appears to rest largely between sarcoid, syphilis and a malignant growth. The clinical picture favors a diagnosis of syphilis, but the early age of the patient is against that possibility.

DR. HARTHER L. KEIM: The condition is probably an infectious granuloma. Sarcoid is a possible diagnosis.

DR. ROBERT C. JAMIESON: Sarcoid does not usually break down so rapidly. The condition may be an infectious granuloma with which the patient has tampered.

DR. WILLIAM G. SAUNDERS: I consider that the condition is probably tuberculous.

PSORIASIS WITH SCARRING. Presented by DR. WILLIAM G. SAUNDERS.

J. L., a man, aged 55, stated that fifteen or twenty years prior to this presentation there were lesions on the elbows and knees, which disappeared after eight years. Two years later they reappeared on the knees, later involving both shins, and almost disappeared under treatment with chrysarobin.

On both shins there were symmetrical, sharply outlined, dark red patches with a small amount of silvery scale, interspersed among numerous thin, soft, pliable scars. There was slight pruritus. A biopsy had been made.

DISCUSSION

DR. HARTHER L. KEIM: This obviously is a case of psoriasis, and the scars may have been produced by treatment.

DR. ARTHUR E. SCHILLER: The scars have developed recently.

A CASE FOR DIAGNOSIS (SEBORRHEIC DERMATITIS?). Presented by DR. ARTHUR E. SCHILLER.

J. M., a schoolboy, aged 13, first observed a pea-sized red area on the left thigh in March, 1932. A second patch appeared on the face, and gradually the eruption became generalized, the back and hands remaining unaffected. The arms, legs, upper part of the chest and ears were most markedly involved, and there was a dry seborrhea of the scalp. The eruption consisted of dry, scaling, erythematous patches, which had been moist, and it was pruritic. The blood count was within normal limits. The basal metabolic rate was —12.

DISCUSSION

DR. HOWARD J. PARKHURST: The eruption on the scalp, ears and upper part of the trunk appeared to be seborrheic, but that on the lower portion of the body suggested a different condition, possibly early pityriasis rubra pilaris. There were no lesions on the hands. Laxatives have been administered repeatedly, and the possibility of a somewhat atypical phenolphthalein eruption may have to be considered.

DR. GEORGE H. BELOTE: Early pityriasis rubra pilaris is a possible diagnosis in this case.

DR. ROBERT C. JAMIESON: I agree that this may be an early case of pityriasis rubra pilaris. Further observation is necessary.

SARCOMA. Presented by DR. GEORGE VAN RHEE.

Mrs. S., a housewife, aged 32, presented a raised horseshoe-shaped lesion on the anterior surface of the lower third of the right leg, freely movable and apparently involving the entire thickness of the skin. There was a small ulcer on the edge, which the patient had produced by scratching. The lesion had been present for one year, having appeared at the site of an injured brown mole. Its development had been gradual, with slight discomfort. The pathologist's diagnosis was "spindle cell sarcoma." Roentgen irradiation was being employed.

DISCUSSION

DR. CLYDE K. HASLEY: The condition is apparently a nevosarcoma or a nevocarcinoma.

BRONX DERMATOLOGICAL SOCIETY

THEODORE ROSENTHAL, M.D., *Secretary*

Regular Meeting, Oct. 20, 1932

ADOLPH ROSTENBERG, M.D., *President, in the Chair*

ALOPECIA AREATA. Presented by DR. MAX BERKOVSKY.

M. S., a Russian, aged 24, a clerk noticed a quarter-sized bald patch in the occipital region about May, 1931. Several other patches soon appeared, and with the spreading of these areas, they all merged until the entire scalp became devoid of hair. There was total alopecia by the end of August, 1931. There was no history of shock, fright or acute illness; there was no baldness in the family. The patient's habits were normal.

The treatment was instituted on Dec. 14, 1931. The patient received 1 cc. of solution of the anterior lobe of the pituitary gland twice a week, 1 cc. of solution of the posterior lobe once a week subcutaneously and 5 grains (0.324 Gm.) of a solution of the whole pituitary gland twice daily. In less than one year of continuous treatment there was complete return of hair.

DISCUSSION

DR. C. GREENHOUSE: How many injections did the patient receive and over how long a period?

DR. BERKOVSKY: The alopecia was of one and a half year's duration. Treatment was started nine months ago with injections of solution of pituitary. Later only a solution of the anterior lobe was given. The patient received no local therapy.

DR. A. ROSTENBERG: Has any other member had experience with this type of therapy?

DR. F. CROSS: I know of a patient under treatment by another colleague. She was given injections of solution of the anterior lobe of the pituitary gland; she became nervous and her menses stopped; the menses lated reappeared.

DR. I. L. LASHINSKY: I know of a patient who had total alopecia of the scalp and the eyebrows. She received injections of solution of pituitary, with very good results.

DR. C. REIN (by invitation): I had a patient who received treatment with solution of pituitary. The hair reappeared, but because of headaches over the parietal region, the treatment had to be discontinued before a complete cure was obtained.

DR. S. FELDMAN: I think that the favorable reports and the unfavorable reports are probably both correct. My impression is that some types of alopecia may be due to an endocrine disturbance, either of thyroid or pituitary origin. I recall a case of alopecia areata in which the hair grew after thyroid therapy. On the other hand, I know of a patient with alopecia who was treated with endocrine extracts without the least benefit. Solution of pituitary is of help in some cases.

DR. H. SILVER: Up to the present I have subjected about two dozen patients to treatment with solution of pituitary. The patients were not selected because of an underlying pituitary condition or other glandular disturbances. The cases represented various types of alopecia, among them the more obstinate cases of alopecia areata. One patient whom I have in mind was a girl of 19 with marked hyperthyroidism, a low metabolic rate and alopecia areata totalis of two years' duration. She has been under my care for more than a year, and only in the last three months is she beginning to show a decided growth.

Dr. Berkovsky achieved an excellent result with comparatively few injections. Even in the cases in which there was a definite pituitary disturbance, Dr. Bengtson had to resort to a large number of injections. Therefore, we have to evaluate cautiously the results obtained in the case presented.

DR. M. BERKOVSKY: I cannot correlate the statement about the production of amenorrhea as a result of the injections of a solution of anterior pituitary extract with other facts. The pituitary gland has two hormones, a sex hormone and a growth-stimulating hormone. The solution of the anterior lobe of the pituitary gland sex hormone should be a menstrual regulator rather than an inhibitor. I cannot state whether the improvement in this case is due to the glandular therapy or whether it is purely coincidental. However, the results are most gratifying, and the method deserves further study.

LATE SYPHILIS. Presented by DR. EUGENE F. KELLEY.

J. H., a man, aged 32, married and the father of three healthy children, said that to his knowledge he had not had any primary or secondary lesions. He stated that he had never been ill until a year before presentation, when an osteomyelitis of the lower part of the left leg developed; it healed promptly.

The present lesion on the right parotid region appeared about six months previously. It was dark red and oval, measuring about 4 by 2 cm. It was slightly raised above the surface of the skin, with sloping borders and sinus openings on the surface, resembling actinomycosis. Under treatment with potassium iodide, the lesion healed about 50 per cent in the three weeks before presentation. The lesions on the lower part of the left leg were hyperpigmented and atrophic, and had arciform outlines.

The Wassermann test of the blood was 4 plus.

DISCUSSION

DR. E. F. KELLEY: This case clinically resembled one of actinomycosis. However, granules of sulphur were not found on repeated examinations. Several cultures showed no growth of actinomyces. Biopsy of a recent nodule showed only acute inflammation.

In view of these findings and the old syphilitic scar on the lower part of the left leg, I think that one can rule out actinomycosis and make a diagnosis of syphilis.

DR. T. ROSENTHAL: The location of the lesion in this patient makes a differentiation of the condition from syphilitic parotitis desirable. However, no definite parotid mass can be palpated, and Stenson's duct appears relatively normal.

DRUG ERUPTION (PHENOLPHTHALEIN). Presented by DR. ISIDOR MOGIL.

The patient, aged 23, single, a furrier, presents large erythematous and purple patches, irregular in outline and of various shapes and sizes. Some of the lesions are bullous, others vesicular or herpetic, especially on the scrotum.

The eruption has persisted for the past three days. The lesions are located on the extensor surfaces of both hands and forearms, feet and ankles, penis and scrotum. Similar lesions appeared a year previously, and subsided within three or four days. The patient stated that he had not taken any drugs.

DISCUSSION

DR. E. F. KELLEY: The patient states that he has received no medication recently. However, he uses a brand of toothpaste, the coloring of which is produced by phenolphthalein, which may account for his eruption.

HEMORRHAGIC SARCOMA OF KAPOSI. Presented by DR. SAM FELDMAN.

This case was presented at the October, 1932, meeting of the Section of Dermatology and Syphilis of the New York Academy of Medicine.

DISCUSSION

DR. S. FELDMAN: When the patient came under observation originally, in June, 1931, he had secondary syphilis. Aside from secondary syphilis, he exhibited a lesion on the palate which was reddish blue. I did not remove any tissue for diagnosis on account of the syphilis.

About eight months later, biopsy was performed. Certain characteristics were seen which, to my mind, were sufficient for a diagnosis of Kaposi's sarcoma. Because of the uncommon location of the lesion, and because no case seems to have been recorded in which there were beginning lesions in the mouth, there may be some dispute as to the diagnosis.

There was a bluish discoloration at the edge of the upper right eyelid, which has now become more marked. To my mind this lesion offers additional proof that this is Kaposi's sarcoma.

DR. L. CHARGIN: It is extremely difficult to make a positive diagnosis in this case. The condition may be Kaposi's sarcoma. The patient presents a bluish patch which is infiltrated, is limited to the palate, and has persisted for a year

and a half. If such a patch were located on the foot or hand, a diagnosis of Kaposi's sarcoma would certainly be considered, but because the lesion in this instance is located on the mucous membrane, one hesitates to make the diagnosis. How can this question be settled? Perhaps the best means of verifying the diagnosis is by making a histologic examination. The histology of Kaposi's sarcoma is indeed not characteristic in all cases. Some clinically typical cases show more formation of blood vessels; some, more cellular elements, and some, increase in fibrous formation; all show a certain amount of hemorrhage. The histologic data in this case fit very well into that of Kaposi's sarcoma. It is not at all necessary that the condition must have its origin on the feet or hands. It is known to originate on the ears and other parts of the face. It may or may not be present on mucous membranes. In making a differential diagnosis, epulis is to be considered. This disease takes its origin on the gums between the teeth and from the periosteum. The histologic elements are not like those in this case. This has no pedicle, which epulis usually has. The condition may be sarcoma, but it seems too benign. The lesion on the eyelid pointed out by Dr. Feldman seems further to confirm the diagnosis of Kaposi's sarcoma.

DR. H. SILVER: Kaposi's sarcoma is not a rare disease. We know what a typical case is like, and where the first lesions appear. It is also known that lesions may appear in the mucous membrane of the mouth. In atypical cases, lesions may appear on any part of the integument. I do not know of a case in which the condition originated in the mouth.

At present, I should favor the diagnosis of angiofibrosarcoma. The fact that the tumor is not malignant is not an indication against this diagnosis. In a case of angiosarcoma which I presented before this society (ARCH. DERMAT. & SYPH. **25**:402 [Feb.] 1932), lesions have been developing for over twenty years without any signs of malignancy. If this case is one of Kaposi's sarcoma, the diagnosis will have to be made at a later date, when more typical lesions will appear.

DR. C. GREENHOUSE: Dr. Satenstein, who studied the slides, expressed the view that the tissue suggests angiofibrosarcoma.

DR. S. FELDMAN: A case of Kaposi's sarcoma in this location has not been described so far as I know. However, because of the evidence presented, one must assume that we are dealing with Kaposi's sarcoma. I intend to treat the patient with radium. I expect to treat both lesions. The assumption is that the eye is more susceptible to radium than the rest of the body, and I do not think there is much danger unless the patient is overtreated.

DR. L. CHARGIN: Treatment should be postponed until a more definite diagnosis is established.

DR. H. COHEN: In a patient under my observation who was treated with radium a cataract developed. I mention this in view of the intention of Dr. Feldman to treat the lesion around the eye with radium.

DR. C. WOLF: Dr. Cohen referred to a patient in whom a cataract developed after treatment with radium. The probabilities are that the eyeball was not properly protected. In treating lesions about the eye, protection must be given with a gold or platinum eye plate over the eyeball. Proper dosage eliminates the danger of injury to the cornea.

JUVENILE DEMENTIA PARALYTICA. Presented by DR. HENRY SILVER.

T. F., a boy, 14 years of age, was first seen in our clinic in August, 1932. About five years ago, his mother noted difficulty in walking, defective speech and restlessness. He is the youngest in a family of eight children. The parents and the other children do not display any clinical or serologic signs of syphilis.

Neurologic examination disclosed a moderate degree of ataxia of both the upper and the lower extremities. The pupils were unequal, and there was a positive Argyll Robertson sign. The speech was difficult, and emotional instability was marked. The knee reflexes were exaggerated. Examination of the eyegrounds disclosed a pale left disk.

The Wassermann reaction of the blood was 4 plus. The Kahn precipitation test was 3 plus. Examination of the spinal fluid at the Vanderbilt Clinic in February, 1931, disclosed seven cells, protein, 37.4 and globulin, 1 plus. The Wassermann reaction of the spinal fluid was 4 plus, and the colloidal gold curve was normal (1111100000).

During the past two years the patient received four courses of antisyphilitic treatment at the Vanderbilt Clinic, given as follows: From Sept. 18 to Jan. 2, 1930, fourteen injections of mercury; during February and March, four injections of 0.1 Gm. of silver arsphenamine each; from April to July, 1930, he received sixteen injections of bismuth, and another course of twelve injections of silver arspfienamine was completed in February, 1931. At the Neurological Hospital he received a course of malaria treatment.

DISCUSSION

DR. L. CHARGIN: In this case it would be interesting to ascertain whether other members of the family have been infected, and, especially, whether the parents are suffering from cerebrospinal syphilis. This has a relationship to a neurotropic organism. In cases of the tabetic form of dementia paralytica or dementia paralytica, not much can be done for the patients from the therapeutic standpoint, and the case presented by Dr. Silver illustrates this point very well.

DR. H. SILVER: The point referred to by Dr. Chargin is important in connection with this case. There are eight children in the family, and this boy is the eighth. All have been examined carefully clinically and serologically. The findings were completely negative in all but the patient presented.

DR. F. CROSS: I should like to know whether or not in tracing the histories of the parents of children with dementia paralytica a neurotropic strain of spirochete has been established.

DR. C. H. MARTIN: I should like to discuss this case, because I have had two recently in which fairly good results have been obtained with arsphenamine therapy combined with cisternal drainage. In both cases there was a positive Wassermann reaction of the spinal fluid. The reaction of the spinal fluid has become absolutely negative. The amount of globulin has decreased. These changes have followed a series of drainages of the spinal fluid. Both of the patients are girls about 16 years old. Both have marked changes in the central nervous system.

Dr. S. Feldman: As to whether these cases are due to a special strain, I shall refer to a case at Lebanon Hospital. The father died of cerebral syphilis. We never saw him, but have this history. We observed the mother and four children. In three children and the mother a positive reaction of the spinal fluid was obtained. One had hemiplegia; two had nystagmus, and the mother had peripheral neuritis. One of the boys, the one who had hemiplegia, died recently; the other case is quiescent. Every one showed some form of involvement of the central nervous system.

DR. C. REIN: In most of those cases, good results were obtained with silver arsphenamine.

DR. H. SILVER: I agree that the prognosis is unfavorable as a rule. Apparently malaria therapy does not benefit the juvenile type of dementia paralytica as compared to the adult type.

PAPULONECROTIC TUBERCULID. Presented by DR. THEODORE ROSENTHAL.

I. G., an American school boy, aged 13, noticed a crop of "pimples" on the legs and arms about five months prior to presentation. One on the leg became ulcerated. Previously his health was good.

On admission to the hospital the patient presented a number of pinhead to split pea-sized erythematous papulopustular lesions on the legs, arms and buttocks, ranging in size from that of a pinhead to that of a split-pea. Some of the lesions had necrotic caps. On the inner side of the left leg was a punched-out, deep

ulceration the size of a quarter. The ulcer healed very slowly under treatment with bland ointments and irradiated petrolatum.

Biopsy of one of the small papulonecrotic lesions revealed chronic inflammation.

An intradermal test with tuberculin 1:10,000 gave positive results. A test with a 1:1,000 dilution of tuberculin was markedly positive, with a constitutional reaction. Roentgen study of the chest gave negative results. The Wassermann reaction of the blood was negative.

DISCUSSION

DR. L. CHARGIN: It seems to me that this case can be better labeled erythema induratum Bazin. In papulonecrotic tuberculid the lesions are much smaller, and the location of the eruption in this case is not that of tuberculid.

DR. C. WOLF: This case is interesting because it shows a lesion on the inner side of the right thigh which is the size of a hazelnut, very red and quite tender and indurated and of recent development. Furthermore, the legs show large scars not found in papulonecrotic tuberculid. I believe that the patient has papulonecrotic tuberculid and erythema induratum scrofulosorum.

DR. F. CROSS: I treated a man, aged 22, who had lesions on the chest and legs, with a 1:100,000 solution of tuberculin, to which therapy he responded very well. I should like to suggest such treatment in this case.

DR. T. ROSENTHAL: This eruption originally appeared to be papulonecrotic tuberculid. Today the patient presents a fresh nodule with erythematous induration, and I agree that the lesions are those of Bazin's disease. He has been given cod liver oil and solution of potassium arsenite; he has improved and gained weight and feels much better generally.

Book Reviews

Treatment of Syphilis. By Jay F. Schamberg, A.B., M.D., and Carroll S. Wright, B.Sc., M.D. Price, $8. Pp. 658. New York: D. Appleton and Company, 1932.

This is the only recent book exclusively on the treatment of syphilis, and the authors bring to its preparation a happy combination of knowledge: a thorough knowledge of clinical syphilis going back, at least in the case of the senior author, to prearsphenamine days, and a unique knowledge among clinicians of the chemistry of the new drugs used in syphilis and of the biochemistry of this field. Its general character is sound and satisfying. In it there are no preconceived notions or theses to maintain; the judgments expressed are founded on the pragmatic base of long clinical experience. The work is excellent in the way in which are developed, simply and clearly, the facts of syphilis as they bear on treatment and the detailed methods of treatment. The novice can read it and acquire a practical working knowledge of all that is involved in the handling of the syphilitic patient. Such a book can be produced only by those who have had large experience and have continuously given thought to the many serious problems involved in the modern treatment of this disease. The style is clear and readable, and the format of the book is all that could be desired. It is a valuable work.

Streptococci in Relation to Man in Health and Disease. By Anna W. Williams, M.D. With an introduction by William H. Park, M.D. Price, $5. Pp. 260. Baltimore: Williams & Wilkins Company, 1932.

This work was referred for judgment to an expert bacteriologist, who happens to be a man of few words. His report was that it contained everything that was known on the streptococci, and that it covered a great deal of pathogenic bacteriology. That is a fair summary of the book. It covers in a well arranged order its entire field, including an extensive bibliography. It is a work that will be found valuable by all dermatologists.

Books Received

THÉRAPEUTIQUE MÉDICALE: V. PEAU, SYPHILIS ET CANCER. Par M. Loeper, G. Milian and others. Price, 50 francs. Paris: Masson et Cie, 1932.

LE MYCOSIS FONGOIDE: GRANULOMES FONGOIDES ET SARCOMES FONGOIDES. Par S. LaPiere. Price, 30 francs. Paris: Masson et Cie, 1932.

IKONOGRAPHIA DERMATOLOGICA: AN ATLAS OF NEW AND RARE SKIN DISEASES. Von J. Jadassohn, Breslau, und Karl Zieler, Würzburg. Price, 15 marks. Berlin: Urban & Schwarzenberg, 1932.

RADIOLOGIC MAXIMS. Harold Swanberg. Quincy, Ill.: Radiological Review Publishing Company, 1932.

HANDBUCH DER HAUT- UND GESCHLECHTSKRANKHEITEN. Von J. Jadassohn. Band XVI, Teil 1: Syphilis. Price, 118 marks; bound 126 marks. Berlin: Julius Springer, 1930.

HANDBUCH DER HAUT- UND GESCHLECHTSKRANKHEITEN. Von J. Jadassohn. Band XVI, Teil 2: Syphilis. Price, 186 marks; bound, 194.80 marks. Berlin: Julius Springer, 1931.

SKIN DISEASES AND NUTRITION (INCLUDING THE DERMATOSES OF CHILDREN). By Erich Urbach, M.D. Authorized English translation by Frederick Rhem Schmidt. Price, $7. Vienna: Wilhelm Maudrich, 1932.

Directory of Dermatologic Societies *

FOREIGN

British Association of Dermatology and Syphilology (Canadian Branch)

J. Frederick Burgess, President, Drummond Medical Bldg., Montreal.
B. Usher, Secretary-Treasurer, Medical Arts Bldg., Sherbrooke St., W., Montreal.

Royal Society of Medicine, Section of Dermatology

A. M. H. Gray, President, 30 New Cavendish St., W. 1, London.
W. N. Goldsmith, Secretary, 6, Upper Wimpole St., W. 1, London.

NATIONAL DERMATOLOGIC SOCIETIES

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

Francis Eugene Senear, Chairman, 55 E. Washington St., Chicago.
Harry R. Foerster, Secretary, 208 E. Wisconsin Ave., Milwaukee.
Place: Milwaukee. Time: June 12-16, 1933.

American Dermatological Association

Fred Wise, President, 200 W. 59th St., New York.
W. H. Guy, Secretary, 500 Penn Ave., Pittsburgh.
Place: Chicago. Time: 1933.

SECTIONAL DERMATOLOGIC SOCIETIES

Baltimore-Washington Dermatological Society

Harry M. Robinson, President, 106 E. Chase St., Baltimore.
M. H. Goodman, Secretary, 401 Medical Arts Bldg., Baltimore.

Central States Dermatological Association

Emmett C. Troxell, President, 74 W. Adams St., Detroit.
William G. Saunders, Secretary, 9203 Grand River Ave., Detroit.

Iowa and Western Illinois Dermatological Association

J. C. Kessler, President, University Hospital, Iowa City, Iowa.
Robert E. Jameson, Secretary, 201 West Second St., Davenport, Iowa.

New England Dermatological Society

Arthur M. Greenwood, President, 416 Marlboro St., Boston.
William P. Boardman, Secretary, 388 Marlboro St., Boston.

Southern Medical Association, Section on Dermatology and Syphilology

Andrew L. Glaze, Chairman, 1928 First Avenue, Birmingham, Ala.
Dudley C. Smith, Secretary, University, Va.
Place: Richmond, Va. Time: November, 1933.

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

STATE DERMATOLOGIC SOCIETIES

Florida Society of Dermatology and Syphilology

Chairman for each meeting is elected from city in which meeting is held.
Frank Wilson, Secretary, 310 Greenleaf & Crosby Bldg., Jacksonville, Fla.
Place: Jacksonville, Tampa, Miami and place of meeting of state medical society.
Time: Quarterly.

Louisiana Dermatological Society

J. A. Devron, President, 150 Baronne St., New Orleans.
M. T. Van Studdiford, Secretary-Treasurer, 912 Pere Marquette Bldg., New Orleans.

Medical Society of the State of New York, Section on Dermatology and Syphilology

Paul E. Bechet, Chairman, 55 Park Ave., New York.
Herbert H. Baukus, Secretary, 925 Delaware Ave., Buffalo.

Medical Society of the State of Pennsylvania Section on Dermatology

Stanley Crawford, President, 200, 9th St., Pittsburgh.
Robert L. Gilman, Secretary, 1930 Chestnut St., Philadelphia.

Michigan State Medical Society, Section on Dermatology and Syphilology

Cyril K. Valade, Chairman, 1604 Eaton Tower, Detroit.
George H. Belote, Secretary, University Hospital, Ann Arbor.

Minnesota Dermatological Society

H. N. Klein, President, 350 St. Peter St., St. Paul.
D. D. Turnacliff, Secretary, 407 Medical Arts Bldg., Minneapolis.

Oklahoma Dermatological Association

William E. Eastland, President, 117 N. Broadway, Oklahoma City.
C. L. Brundage, Secretary, 616 Medical Arts Bldg., Oklahoma City.

Texas Dermatological Society

T. J. Calhoun, President, 1719 Pacific Ave., Dallas.
Everett R. Seale, Secretary, 1215 Walker Ave., Houston.

LOCAL DERMATOLOGIC SOCIETIES

Atlanta Dermatological Society

Francis G. Jones, President, 384 Peachtree St., Atlanta, Ga.
Charles A. Wilkins, Secretary, Medical Arts Bldg., Atlanta, Ga.

Bronx Dermatological Society

Adolph Rostenberg, Chairman, 152 E. 179th St., New York.
Theodore Rosenthal, Secretary-Treasurer, 115 W. 86th St., New York.

Brooklyn Dermatological Society

Louis J. Frank, President, 1367 Eastern Parkway, Brooklyn.
George F. Price, Secretary, 884 Lincoln Place, Brooklyn.
Time: Third Monday of each month except June, July, August and September.

Buffalo Dermatological Society

Herbert H. Bauckus, Presidennt, 925 Delaware Ave., Buffalo.
William F. Hoover, Secretary, 333 Linwood Ave., Buffalo.

Chicago Dermatological Society

Michael Ebert, President. 25 E. Washington St., Chicago.
E. A. Oliver, Secretary, 55 E. Washington St., Chicago.

Cincinnati Dermatological Society

Ralph R. DuCasse, President, Carew Tower, Cincinnati.
Raymond G. Senour, Secretary-Treasurer, 19 W. 7th St., Cincinnati.

Cleveland Dermatological Society

E. W. Netherton, President, Cleveland Clinic, Euclid Ave. and E. 93d St., Cleveland.
H. G. Miskjian, Secretary, Rose Bldg., Cleveland.

Detroit Dermatological Society

Emmett C. Troxell, President, 74 W. Adams Ave., Detroit.
William G. Saunders, Secretary-Treasurer, 9203 Grand River Ave., Detroit.

Los Angeles Dermatological Society

Samuel Ayres, Jr., Chairman, 2007 Wilshire Blvd., Los Angeles.
Louis F. X. Wilhelm, Secretary, 1401 South Hope St., Los Angeles.

Manhattan Dermatologic Society

Fred Wise, Chairman, 200 West Fifty-Ninth St., New York.
Mihran B. Parounagian, Secretary, 126 E. 39th St., New York.

Montreal Dermatological Society

J. F. Burgess, President, Drummond Medical Bldg., Montreal, Canada.
B. Usher, Secretary-Treasurer, Medical Arts Bldg., Sherbrooke St., W., Montreal, Canada.

New York Academy of Medicine, Section of Dermatology and Syphilis

A. Benson Cannon, Chairman, 371 Park Ave., New York.
Louis Chargin, Secretary, 1 W. 85th St., New York.

New York Dermatological Society

George M. MacKee, President, 200 W. 59th St., New York.
Edward R. Maloney, Secretary, 853 7th Ave., New York.

Omaha Dermatological Society

H. C. Sumney, Chairman, 1011 W. O. W. Bldg., Omaha.
Donald J. Wilson, Secretary, 1216 Medical Arts Bldg., Omaha.

Philadelphia Dermatological Society

Frederick D. Weidman, Chairman, 1930 Chestnut St., Philadelphia
Robert L. Gilman, Secretary, 1930 Chestnut St., Philadelphia.

Pittsburgh Dermatological Society

Claude B. Norris, Chairman, 244 Lincoln Ave., Youngstown, Ohio.
Frederick Amshel, Secretary, 3401 5th Ave., Pittsburgh.

St. Louis Dermatological Society

Richard S. Weiss, President, 3720 Washington Blvd., St. Louis.
M. F. Engman, Jr., Secretary-Treasurer, 3720 Washington Blvd., St. Louis.

San Francisco Dermatological Society

Charles Schoff, President, 1127, 11th St., Sacramento, Calif.
John M. Graves, Secretary, 909 Hyde St., San Francisco.